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METHODS USED TO CONDUCT A PRELIMINARY CUMULATIVE RISK ASSESSMENT FOR ORGANOPHOSPHATE PESTICIDES

February 6, 2002

[8:30 a.m.]

SHERATON CRYSTAL CITY HOTEL
1800 Jefferson Davis Highway
Arlington, Virginia 22202

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DR. KENDALL: Good morning, this will convene the meeting of the FIFRA Scientific Advisory Panel to continue our discussions on methods used to conduct a preliminary cumulative risk assessment for organophosphate pesticides. My name is Ron Kendall. I'm the chair of the Science Advisory Panel and will be chairing this session.

I'd like to again thank EPA for being ready, and I thought we had an excellent and productive day yesterday. And I'm looking forward for the continuation of our discussion today.

We have several new panel members that are seated; therefore, I will, as a matter of protocol, ask the Panel to reintroduce itself in total. I'd like to begin on the far right and then move around. And, please, for the record, state your name, affiliation, and expertise if you would briefly.

DR. CAPEL: My name is Paul Capel. I'm with the US Geological Survey Water Resources Division. My expertise and water chemistry for the drinking water exposure part.

DR. ENGEL: Purdue University. My expertise would be in the hydrologic water quality modeling area.

DR. BULL: I'm Dick Bull with Washington State University. I'm a toxicologist.

DR. DURKIN: Pat Durkin with Syracuse Enviornmental

Research Associates. I am a risk assessor and I've worked with the Agency in development of methods for mixtures risk assessment.

DR. HARRY: Jean Harry, National Institute of Environmental Health Sciences in North Carolina. My research area is in neurotoxicology.

DR. CONOLLY: Rory Conolly, CIIT Centers for Health Research in Research Triangle Park, North Carolina. I'm interested in mechanisms of toxicity and risk assessment.

DR. RHOMBERG: Lorenz Rhomberg, Gradient Corporation, and also the Harvard School of Public Health. I'm interested in quantitative risk assessment methodology.

DR. MCCONNELL: Gene McConnell. I'm a veterinary pathologist-toxicologist. My area of expertise is in the design, conduct, and interpretation of animal bioassays.

DR. ROBERTS: Steve Roberts; toxicologist; University of Florida.

DR. PORTIER: Chris Portier, National Institute of Environment Health Sciences in Research Triangle Park, North Carolina. I direct the environmental toxicology program and manage the national toxicology program. My area of expertise biostatistics and risk assessment.

DR. ZEISE: Lauren Zeise, Kelly P. Office of Environmental Health Hazard Assessment. My expertise is in risk assessment.

DR. RICHARDS: Pete Richards, director Of the Water Quality Lab at Heidelberg College in Ohio with expertise in exposure patterns in agriculture systems in the upper Midwest and the statistics applied to those.

DR. ADGATE: John Adgate, University of Minnesota School of Public Health, exposure analysis and risk assessment.

DR. REED: Nu-May Ruby Reed, California Environmental Protection Agency, Department of Pesticide Regulation. I do pesticide risk assessment.

DR. FREEMAN: Natalie Freeman, Robert Wood Johnson Medical School and the Environmental and Occupational Health Sciences Institute in Piscataway, New Jersey. Residential and children's exposure.

DR. MACDONALD: Peter MacDonald from the Department of Math and Statistics at McMaster University in Canada. General expertise in applied statistics and model fitting.

DR. HEERINGA: Steve Heeringa, the Institute for Social Research at the University of Michigan. I am a biostatistican. My specialty is in population-based research.

DR. KENDALL: I'm Ron Kendall from Texas Tech University. I direct the university's Institute of Environmental and Human Health. My area of expertise is in environmental toxicology and risk assessment.

I'd like to now introduce our designated federal official from EPA, Mr. Paul Lewis, for any administrative procedures that he needs to inform us on to get going today. Paul.

MR. LEWIS: Thank you, Dr. Kendall. And again thank you again for agreeing to serve as our chair for this challenging and interesting meeting over the next four days with our Scientific Advisory Panel. I want to thank the members of the panel to agreeing to serve and we're looking forward to your upcoming deliberation and challenging discussions beginning with what we had yesterday and carrying on today and beyond and for new members that have joined us this morning for discussion on vary exposure considerations.

I want to remind everyone again that this meeting follows of the guidelines of the Federal Advisory Committee Act. This is an open meeting. There's an opportunity for public comment. All the materials for the meeting will be available in a public docket. In addition, the primary background materials and our subsequent report that serves as meeting minutes for discussion during this week will be available in

the docket edition on our SAP web site.

Thank you again. I'm looking forward to both a challenging and interesting over the next few days. Dr. Kendall.

DR. KENDALL: Thank you, Paul. Yesterday was a very aggressive and forward-looking day. We actually got much further than we thought we would. Therefore, today, we are at the point of assessment of food exposure in terms of Session 2 as we continue our review.

Dr. Perfetti, would you like to introduce your group or Margaret, either one of you?

DR. PERFETTI: Thank you, Dr. Kendall. First of all, I'd like to welcome the panel to today's session on food and drinking water. And again I would like to thank the panel for all your valuable past advice on the total assessment as well as yesterday's very interesting discussion on hazard and dose response.

For the food presentation, Dr. William Smith, sitting to my left; and Dave Miller will provide that presentation on food. Presentation on water will be performed by Kevin Costello and Nelson Thurman.

I have a few points that I'd like to make, Dr. Kendall, before we continue.

DR. KENDALL: Very well.

DR. PERFETTI: As mentioned yesterday, we intend to address all of the points brought up yesterday during the public comment period. We intended to address many of those points anyhow in our presentation; but we have modified them such that we think we will be able to speak to all of them.

To that end, we heard yesterday that OPP would be receiving an OP cumulative assessment using the CARES software. OPP has also contracted the Lifeline Group to perform a cumulative risk assessment for the organophosphate pesticides.

This project has three components. The first is to modify the Lifeline version 1.1 software as required to allow estimation of cumulative exposure and risk for the organophosphate pesticides. In addition to modifying the software, Lifeline Group will perform a cumulative risk assessment for the OP and revise the user and technical documentation to the Lifeline model so that it can be used by all of the risk assessment community. We have done this in order to -- basically, we thought ahead. We did this in order to have yet another software package for cumulative risk assessment.

And, finally, I cannot stress strong enough that OPP has no intention of exclusively endorsing a particular model for estimating pesticide exposure and risk. We'll accept any and all risk assessments

conducted in accordance with EPA and OPP guidelines and performed with an appropriately peer-reviewed model. That can never be stressed more strongly or often enough.

Thank you, Dr. Kendall.

DR. KENDALL: Thank you. Well, at this point, we can begin. Let's go ahead and begin the presentation. Dr. Smith.

DR. SMITH: Good morning. This is an outline of what I plan to discuss today. I want to cover three general areas in this discussion. First, I would like to summarize the exposure inputs to the cumulative food assessment. This includes the residue data, primarily from the PDP monitoring program for food consumption data from the USDA continuing survey of food intakes by individuals.

Secondly, I'll briefly review the residue adjustments involved in the cumulative assessment. These are fairly simple calculations compared to what we dealt with yesterday. This involves a conversion to index equivalent residues, that is, methamidophos equivalence, the relative potency factor method.

And then last, we'd like to review the preliminary assessment as published in December which is a probabilistic exposure risk assessment using the DEEM software.

Also, I will include some analysis of the important assumptions

that were incorporated in the exposure calculations and the beginnings of the analysis of important contributors to the exposure distribution.

Essentially, all the residue data that we used in this assessment are from the PDP Program. We, also, considered FDA monitoring data, but this was primarily as background. There were only very limited uses of it on a quantitative basis. All of these data are available on the internet at these Agency's internet sites.

The OP active ingredients that are included in this assessment are all included in the PDP monitoring program. What you see here are essentially the parent active ingredients. PDP also analyzes for important metabolites of these chemicals and degradates. And they are also included in the assessment. I think between the span of 1994 to 2000, PDP has done significant analysis on maybe 70, or approximately 70, OPs, either parent active ingredients or metabolites. The extent of how we use these data are the extent of the availability as well as how we use is available in our preliminary document in the appendices.

We do not include cancelled uses in the assessment nor do we include violative residues. Now these are tolerance-exceeding residues or residues from nonregistered uses. Violative residues are generally infrequent and for the most part at low concentrations. And

both PDP, our primary source, and for that matter, an FDA data, which is designed to enforce tolerances.

I do not have an exact accounting of our the effect of our omission of these violative residues. But it will be available with the final assessment. But I can offer some general statistics.

In the most recent PDP data, tolerance-exceeding residues are on the order of .2 percent of the analyses. And residues from nonregistered uses account for a little bit over 1 percent. The FDA monitoring, which one would expect to have more violative residues since it is designed to analyze raw commodities close to their source, has a little bit more. It has with domestic, approximately 1 to percent violative residues; and import, closer to 4 press.

So for just as a general background response to public comment about this, that is what we generally see in all the monitoring data. Also, the data bases that are available on the internet from these agencies as well as our data -- let me retract that. Our data do not flag the violative residues, but the data bases as available from USDA and FDA do. So one can easily pick out of the residues. There is a field in the data base that identifies these.

There has been approximately 50 different foods that have been analyzed in the PDP Program since 1994. And this is, of course,

counting some processed forms such as canned, frozen, this sort of thing. All of these foods are included in the assessment. But some specific chemical commodity combinations have been excluded to account for cancellations or tolerance revocations and phase outs of uses.

The residue data for these foods as supplied by PDP have been adjusted by processing factors where suitable to include all the related food forms found in the CSFII survey. Again, for example, using a raw commodity with a processing factor to estimate residues on a cooked, canned, frozen form, possibly a juice or dried form.

These data were extended to the extent possible by translation. And in this case, it was done to food crops that had similar use patterns. I will come back to these crops a little later in the discussion of the preliminary assessment.

These are based on SOPs that we have developed for single chemical assessments, and they are limited to crops for which use patterns are similar. So we done translate a chemical that would not be appropriate to the other commodity.

Although, we primarily use FDA's background, there are some exceptions. Eggs and seafood were included in the assessment. And in both cases based on a long history of analysis by FDA with

negligible appearance of OPs. It was our judgment that we could include these in our assessment as negligible residues.

Also, we included, based on the FDA total diet study, which is a study -- the available data now on the internet goes through 1991 to 1997. These are market basket analysis -- actually, at-the-plate analyses of prepared foods. Based on these assessments, it was our professional judgement that we could include an estimate in our assessment for the meats: Beef, pork, sheep, and goats. This is an conservative estimate of residues based on the maximum values determined from the total diet study. It's the only exception in the assessment in which we use what one may consider a default assessment. As it turns out, we have seen no real impact of this on the total assessment. These values are still very low.

There are some other foods that were assumed negligible, although we did not have extensive monitoring data. These are sugars and syrups that are highly processed and refined. Based on that fact alone with information we have on related commodities, led us to conclude that we would not expect OPs to be present in these. So they were included as negligible in the assessment, also.

Now, as a means of getting one perspective of assessing what portion of the diet we're covering by these data that I've just

summarized, we ranked the foods as consumed by children from the CSFII survey on a per capita basis in a descending order. And then for each food we assigned it a percent value based on the total consumption.

And what I have here in the table is an indication of what proportion of the per capita consumption is covered by the things I just summarized.

In this case, the PDP data, both of the raw commodities and any processed commodities that we translated these data to, account for approximately 86 percent of the diet. The translation that indicated, I showed you, about 20 different crop names up there, account for only 1.3 of the per capita consumption. The data, the FDA-supported data on eggs and fish and meat, account for approximately 6 percent of per capita consumption.

Our assumption of negligible for sugars and syrups is another 3 percent. And this leaves approximately 4 percent of the food per capita consumption that we have not included in the assessment.

Again, with this ranking of foods for children three to five in this case, the top 30 foods in this ranking are included in the assessment. And the top cumulative 95 percent of this diet that is comprised of 556 foods, of 52 those are included. The ones I excluded

are dried beans, some corn-processed commodities and onions.

Other foods. Those and the other foods that are not included, we do not expect to impact significantly on the assessment; although we do have means to still test this and it is ongoing. Many of these are highly processed or blended foods; therefore, you wouldn't expect to have very high levels of these chemicals. And based on FDA data and chemical registration data, we believe that all these would have infrequently detected residues or low levels.

Moving on now to the residue adjustments. We're all familiar with our way of dealing with exposure and risk here. We talk in terms of margins of exposure, which would be a point of depart divided by an exposure. The point of departure is in this case is a benchmark dose 10. The exposure, of course, is composed of residue and consumption.

The residues for this assessment are the cumulative residues. We can converted chemical-specific residues on food samples to a common residue. And this is an index-equivalent residue. This was done on a sample-by-sample basis.

So an index-equivalent residue on a given PDP sample would be estimated by multiplying that residue value by any applicable processing factor and by its relative potency factor -- its potency

relative to methamidophos. And these residues would be summed for each sample to become the cumulative residue in terms of methamidophos.

Then these cumulative residues become inputs for the assessment. Either as distributions of cumulative residues with each number in the distribution representing a PDP sample or average cumulative residues for some highly blend foods.

For our consumption modeling we used the CSFII, years '94 through '96 as supplemented in 1998. There are over 20 thousands participants in this version of the CSFII. The surveys were conducted. It was 2 days that were approximately 3 to 10 days apart. And this does contain a 1999 supplemental children's survey where an additional 5,500 children from birth to nine years old were included.

This survey is a significant increase for the number of children as compared to the '89-'91 survey which we have been using at OPP for you all of our single chemical assessments to date. This is illustrated in this table which compares the number of children of various age groups between the '89 to '91 data and the more recent. You can see, for example, for children one to two, the number of individuals is increased from 574 to 2,179.

The assessment, as currently published, includes four population

groups. Other age groups can be assessed easily, but none has exposure estimates that exceed these groups we have. And the children one to two are the highest exposed.

The exposure assessment models that we're using in this assessment are DEEM and Calendex. My comments are going to be restricted to the assessments as conducted with DEEM. David Miller will be discussing some issue after I'm finished that incorporating the Calendex. And he will highlight differences at that time.

DEEM combines residue and consumption distributions in a Monte Carlo-like procedure to produce a distribution of one-day exposure and associated margins of exposure.

We're using the FCID version of DEEM, which has recently been released. This uses EPA's food commodity and intake data base and commodity definitions. This may lead to some confusion on the part of one who is reading through our assessment as published because this came at a fairly late date in our assessment. And you will find that we are referring to food forms as defined in the earlier CSFII. But when we get to the actual assessment, we translate these to the FCID form.

And, of course, among the differences in these, that is, one difference in this FCID version of DEEM is that foods do have

different codes and many of them have different names. There are some separate breakouts, for example, commercial baby foods are broken out for each appropriate commodity.

Another significant difference is that this version of DEEM uses publicly available recipes for relating the foods consumed to the raw commodities or the values that would be plugged into the for estimating exposure.

So this is the preliminary assessment as published in December the 3rd. And this plot is a representation of the entire distribution from zero to 100 percent of the exposure distribution. The top line of the graph represents the BMD10 of .08 milligrams per kilogram per day. The bottom line represents a value that is one million times lower than that.

And there are four populations on this graph. If we can move to the next one. This focuses in on the top 10 percentile of the exposure range. And from this, I think you can begin to see that children one to two are the most highly exposed population group. And then with the specific numbers broken out for these four populations between the 90th and 99.9th percentile.

By June of this year we expect to have completed all the refinements of the preliminary assessment and this includes, of course,

consideration of all the public comments as well as some QA on our own part, changes we know need to be made. So this is very -- we're very actively pursuing this.

We, also, have been conducting sensitivity analysis to gauge the relative importance of the assumptions that have gone into the inputs. We first revealed some of these in the case study that we presented to the panel in December of 2000. And in principle, our results have not changed from that in terms of the validity of those assumptions as we tested them. And we're, also, beginning the process of the interpretation of the results.

So next. Could you go back one. So, first, I would like to show you a few results looking at the potential effects of input assumptions and refinements on the assessment. Look at the effects of translation of PDP data to other foods using processing factors to estimate residue.

These data on this slide if you recall I showed you about 20 foods for which PDP data were translated because we feel they have similar use patterns. And, of course, this is subject to question always. This is a test of just what effect -- if we were making wrong assumptions, what effect this would have on our assessment. And this somewhat confirms our rankings that we had from the per capita

consumption, too, the foods to which we translated make up a relative small proportion of the consumption and the total exposure. At the higher percentiles, there is very little difference in the assessment if one removes the assumption of OPs from all the translated foods. And that's what this represents.

We have a particular case here of a translation of data to a process commodity. In this case, we do not have processing factors or other information input into the model for conversion of OPs from the raw commodity to the baby foods. And, of course, we wanted to test and see how this assumption could effect our end result.

And with the new version of DEEM, one can selectively remove the contribution from all the baby foods. We did this for children one to two. And it confirms that there is essentially no effect on the assessment. This is probably not totally unexpected.

We, also, have done the same thing for children less than one. And there is no effect because they eat more baby food. However, children less than one as a group have a lower exposure than children one to two.

This is somewhat of a boundary on all of our processing and other extrapolations that we made. In this case, the top line, the top row, is the full assessment. And the other row of information

indicates that a similar assessment in which we removed all translated commodities and all extrapolated data so the only information, the only OPs incorporated into the assessment, are directly related to PDP analyses.

So there are no assumptions of processing factors; there are no processed commodities unless PDP analyzed that processed commodity. And there were no translated crops. And we felt this was interesting to just sort of set a boundary on what we could expect to accomplish with a number of refinements that we want to make to these assumptions.

This is the previous slides in a graphical form the top 15 percentile of exposure. The top line represents the full assessment and, also, coinciding on it in this scale is using only not translating to other crops. And the lower lines represents removing all extrapolations.

Now, we gave you a revised question, one for food. This is partially the result of the limitations in time we have in doing some of these analyses. And we were working on this part of the assessment at the time we submitted the question. Based on the complexity of what we were getting and the fact we did not have time to finish some of the analyses, we choose to focus on some later things we're going to show

you. But I wanted to show you this anyway because it has come up and it has been put on the internet.

In this case, we have questioned all along what the impact might be of the fact that our PDP data ranges in the time frame of 1994 to the year 2000 now. That's approximately seven years of data. Some of the information comes from only the earlier portion of that time; some from the later; some is spread across the seven years. We have as little at one year of data for a food and as much as five years. We wanted to evaluate the later data to see if they better represent the current use practices.

This is incomplete; but at least in terms of an assessment, I can show you how removal of older data, to the extent that only the most recent two years maximum was included for any given food, has some effect on the upper portion of the distribution. Maybe not a dramatic effect, but it is shown in this slide.

So this analysis is not complete. We need to carefully look at use pattern changes that have accompanied this. And we can, also, look at specific chemicals that were removed by removing the older data. So these are complex factors. We know, we did know, we were working with multiple distributions representing different segments of time.

Now for the final portion of this, I'd like to briefly summarize our progress so far. I want to first qualify this by saying that we are beginning to analyze critical exposure contributors; however, we're doing this on the preliminary data. So for this reason, although the process is of interest to us and we want as much input that we can get on this process and how we can interpret it, the actual results that we're getting at this point we're sure may be subject to some change; therefore, we're going to speak in terms of pseudonyms again. I apologize for that.

This case we were looking at -- could you back up one? I should point out that the DEEM software has a critical exposure commodity analysis incorporated in it. This is a means of looking at the top much as 5 percentile of exposure to get an idea of which food commodities are food are contributing, which food consumptions are actually contributing to that part of the distribution. And we're looking at this to get some idea of which foods and, also, which chemicals are important. And we also, by keeping track of our sample analysis on a sample-by-sample basis, we also have a history on all these numbers. So we can go back and actually get sample details, such as the origin, whether it's domestic or import data and whether sample was taken in 1994 or the year 2000.

So working with the preliminary results and looking at, in this case, we're looking at the area of the distribution between the 99.8th percentile and the 100th percentile of exposure. And the critical commodity exposure element does give you a listing of sort of a descending ranking of foods that are contributing to that portion.

And over in this range, under the conditions of our run, which, again, are preliminary, we had over 60 percent of the contribution to this area was coming from three foods in all their forms. This could include the raw commodity; it could include juices, dried forms, sauces. It's three food crops that are contribution to this. And we examined the impact of removing these residues from the assessments to see how this may impact the upper part of this distribution.

Again working with children one to two, we looked, we compared the full assessment. Two runs in which we removed singly each one of the foods. Food A was the most abundant in this part of the distribution. And if you remove only Food A, that second row illustrates what effect that has on the distribution at the higher end. Removing only Food B, there's less of Food B; the effect is less. And same sort of thing with Food C.

Taking both A and B out, again, depending on one's perspective, probably not a lot of change. It required removing all three foods in

all their forms to affect the change at the very top end of the distribution of a two-fold change.

And this is just illustrating graphically what we have here that as you go toward the lower parts of the distribution, effects can be observed. But at the very top end of the distribution, it's difficult at times to tell the significance of the differences.

And, again, just another way of looking at this. Also, I've included the 50th percentile here which may not be in your background materials. Just comparing the ratio of the MOEs at these different points in the upper part of the distribution, you can see that the upper portion of the exposure distribution is not affected very dramatically by removing of these major contributors singly. And, again, to get a two-fold change, required all three.

So our interpretations of the risk results are a little premature to do that. But we do conclude at this point, that the PDP residue data do cover the major food consumption items. We, also, based on what we have so far, further refinements of the PDP data are not likely to drastically alter the results at the higher end of exposure distribution. And a rather nebulous conclusion here: Complex factors are contributing to the exposure distribution.

There was, also -- if you back up, there's also a calendar-based

exposure which we used for food as well as the other pathways of exposure. And David Miller will discuss that next.

So now I think probably that ends my part of the presentation.

DR. KENDALL: Any points of clarification? Thank you, Dr. Smith. Very good. Any points of clarification from the Panel before we move to the next section? Dr. Bull.

DR. BULL: This last piece is a little counter-intuitive to me; maybe not to others. I think you were saying is the higher the exposure, the less able you're able to account for causing that exposure. That's my interpretation of what you're saying. I would have thought -- and just to give you a minute to think -- that something would be driving that very high exposure and that's not what you seem to be ferreting out of that data.

DR. SMITH: In a sense, that's what we're asking you is how do we interpret these results to help us however you can. As you go to lower parts of the distribution, of course, the total exposure is decreasing to very low values. So for that reasons, there's not much difference.

DR. KENDALL: Go ahead. Dr. Portier.

DR. PORTIER: Following up on that same question, it seemed to me that there's two possibilities for what could drive these margins

of exposures and reducing them for single commodities. One is the commodity which very seldom has an OP level in it, but that OP level is rather high when it's in there. That would contribute to the high end of the tail of the distribution.

The other possibility is a commodity that has a fairly common OP contamination in it but at a lower level. And it seems to me the analyses you focused on for the commodity here is to find the rare events. Did you know that when you went into that, or have you thought about looking at reducing the entire distribution by finding potential commodities that have low levels by consistently there?

DR. SMITH: Yes, we have thought about that. And there is a companion part of this output from the DEEM in that you actually see those highest exposure events. What I was talking to you about was a summary of these highest events. And but we can also pick out the actual food consumptions that contain the highest residue or the highest consumption value. And we are trying to compare those. And it is a little less straight forward.

At this point, we can't say much beyond what we've done -- it is easy to pick out the top foods, you know, the ones that are coming to the top of the assessment. And they of course, you're right. There is a combination of having and some of them have a high percentage of

residues and/or high residues. Both factors are there. In addition, of course, to whether it's a high consumption or not.

DR. KENDALL: Dr. McConnell,

DR. MCCONNELL: Two questions. First, are we are allowed to ask what A, B, and C are? Oh, we have to go to the top.

MS. MULKEY: We made a judgment that we could obtain the science thinking about this without identifying at this stage.

DR. MCCONNELL: Well, sure.

MS. MULKEY: Because there is a real market place, we thought it was prudent we get the benefit of an enhance understanding of the science before we did that.

DR. MCCONNELL: I guess the PC cops are out today.

What has been your experience over the past seven years? Have the percentages of exceedence been going up or down, or finding that in the particular commodity has it been increasing or decreasing with time for the, if you will, for the problematic commodities?

DR. SMITH: Exceedence, well, there's exceedence of tolerance.

DR. MCCONNELL: Maybe I didn't use the right term. I think you know what I mean.

DR. SMITH: Yeah, you mean just the occurrence of these.

DR. MCCONNELL: Yes.

DR. SMITH: In general, the terms are hand to pick out based on the information we have, but there is a decrease. So from 1994 through the year 2000, one can see the appearance of a decrease of occurrence. This is -- I hesitate to say that that's a fact because this is being observed without extensive statistical analysis. And of course, we are interested in that and part of our goals are to decrease the levels on foods.

DR. DURKIN: You have identified the top three foods. You have, but we can't know it. What about the top three chemicals? Is there a parallel analysis where you look at it by chemical over the total diet so you can identify the chemicals that are there?

DR. SMITH: We are also looking at the chemicals in these top foods, and we can track that because of the way we did the distributions. We kept it tied to a PDP sample ID. And we do know the processing factors and the origins of the samples. And in these three chemicals -- I can say there are more than three chemicals involved in those three foods; yes.

DR. DURKIN: I just want to be rear clear here. There could be a parallel analysis where essentially you could spit out a vector of the chemicals combined over the total diet. So if we wanted to identify, as

I'm sure you do at some point, what are the specific chemicals that contribute most to risk and how is that laid out? Is that possible with the software you have now?

DR. SMITH: Yes, it is. That is also underway. I choose not to discuss it. We can selectively remove a given chemical's contribution from the cumulative assessment. We can do it for a given food chemical combination or just across the board. And that's also actively in progress. But I just don't have -- I don't have any anything really to relate to you on that at this point.

DR. KENDALL: Dr. Rhomberg. Dr. Durkin, any further clarification? Dr. Rhomberg.

DR. RHOMBERG: I'm stepping a little bit out of my realm of expertise here. It seems to me that one could say that it could be that all sort of common diets are the same and every eccentric diet is eccentric in its own way. So that might say that it would be a mistake to focus on the single chemical or single food that causes the biggest contribution to risk if that's something that's ubiquitous and unavoidable.

It's sort of raising the baseline for everybody. And then the people that have various odd combinations of things, which would be very different for each of the different people, are the things that are

causing peaks and throwing a certain individual into the tail of distribution one way or the other. That would be very important to know for risk assessment purposes.

Is there a single thing that you can do? Is the way to avoid problems that are caused by single unusual events in people because of an exceedence or very eccentric diet is the way to handle that, lowering the level of everybody, sort of lowering the average level so that the peaks don't go higher or to attack the peaks particularly?

As I say, this is out of my realm both from the point of view of assessing diets and from risk assessment. But I think it would be important to pull out those kinds of observations from these things. So that in a way, when you're looking at the peaks, maybe the thing isn't the biggest contributors; it's the ones that are most different from the main stream of people farther down in the distribution and are there consistencies there that can be got at.

DR. PERFETTI: Dr. Rhomberg, if I understand correctly, I think what you're asking is do the peaks represent unusual consumptions.

DR. RHOMBERG: Unusual consumptions or unusual residues, whatever. Just things that are -- it's got to be unusual something because there has to be some reason why they go up into the peak.

DR. BULL: Otherwise you wouldn't get that distribution that we just talked about. I was right.

MR. MILLER: The CEC does print out essentially those individuals in the upper tails of the distribution. It lists out the consumption and lists out the residues associated with that. And what we do is look through that and get an idea of what's doing it. Is it unusual consumptions entirely by one commodity or unusual residues or such. So that is something we do look into in evaluating these things and judging their reasonableness.

DR. SMITH: You know, to not be totally precise in describing this, it is a very complex and even some of our single chemical assessments maybe were not that different in their complexity. But in this case, we are -- we do have the overlapping situation of distribution of consumption, a distribution of a variety of possible chemical uses. So more than one chemical is involved. And there's not necessarily a direct correlation between the frequency of occurrence and the relative potency of that chemical because these are all adjusted relative to methamidophos and we have a wide range of potencies in the chemicals over a few orders of magnitude.

We have, to our way of thinking, a fairly complex overlay and the possible time frame consideration, a possible, fairly complex

overlaying of potential distributions. And we are look thing for what are the single things we can do to interpret what this means. And to this point, it's not necessarily a single thing; it's a combination.

DR. KENDALL: Dr. Portier.

DR. PORTIER: I was going to try to clarify Lorenz's comment. But I think it's more appropriate for a discussion later on.

DR. KENDALL: I agree. Dr. Heeringa.

DR. HEERINGA: I have a very quick question about the mechanism of the simulation where you remove foods A, B, and C. When you do that in the simulation, do you literally strike those foods out of the sample child's diet; or do you sample children who consume those foods on that day? In other words, is there a replacement of other diets that's taking place in the simulation?

DR. SMITH: We're removing the OP contribution to that diet.

DR. HEERINGA: You actually sample the child. And if it happens to be a contribution A, B, and C, so you're essentially lowering an expectation the overall residue consumption.

DR. SMITH: Correct.

DR. KENDALL: Dr. Freeman.

DR. FREEMAN: Two things. When you did this, are you only looking at commercially used pesticides as opposed to residential

fruits and vegetables that are treated? And the second thing is, a number of these commodities, based on the data that we were provided with, are produced in very specific regions. You know, they're either warm weather crops or they're cold weather crops. And so you may have three areas of the country that are generators of, say, one of these crop items.

Have you looked at the differences in pesticides according to the regions from which the samples were obtained? And have you tried to do some sort of weighting based on some sort of distribution across the regions as to how it's going to impact on the pesticides in these foods?

MR. MILLER: The assumptions in this assessment is that PDP does sample proportionate to a national basis proportionate to production. So if 20 percent of crop A is grown in California, or consumed in California, 20 percent of the samples would be from there. So overall, on a national basis, yes, it is proportionate to that.

In terms of looking at regional residues, for example, we assume essentially it's a national distribution of the commodity. So we don't look at specific regions and don't look at specific residues in specific regions.

DR. FREEMAN: Yeah. I'm a little concerned about that

because you see a constellation of pesticides in one region for say apples that you may not find in another region that grows apples. They have one or two that are the same, but there may be differences. And that might impact your results.

DR. KENDALL: Dr. Adgate.

DR. ADGATE: I'm curious. What's the rationale for removing the violative residues?

DR. SMITH: Should I pass that to the end of line or try it myself?

MS. MULKEY: In pesticide regulation, there's always the challenge of whether you regulate to violations or regulate on the basis of the assumption that people comply with the law. It's not unique to this situation. We face that issue a lot. And if we believe that violations are endemic, that there's sort of an inherent aspect of the lawful use, we will consider violative scenarios. I'm talking now generally, not in this one. I think we do not have a basis in these examples in believing that the violations predictable, sustainable, sort of unavoidable by product of lawful use.

But if we did or had some basis to, then that would be the situation in which would typically take into account violations. This is not a policy we developed just for this approach. That's been our

longstanding approach to the way we thought about pesticide regulations. And it involves not just foods but other exposure situations, too.

DR. KENDALL: Dr. Portier. This is the last question.

DR. PORTIER: No, this is four or five. I was waiting to see if anyone else would ask them. Again, hopefully, these are just clarification questions. In what you just presented, those are single day resamples for single-day diet; is that correct?

DR. SMITH: Yes. But it's using both days of the diet.

DR. PORTIER: Okay. I don't understand that. Run that by me again.

DR. SMITH: They are single-day exposures, but they are obtained by using a survey that is composed of two separate days.

DR. PORTIER: And in the two-day survey that you're using, you're just using the one of the days as the resampling for food consumption.

DR. SMITH: No, in DEEM, both days are used.

MR. MILLER: The count is separate. I'll get into it a little bit in my presentation. The account is essentially separate people. In the diet food Person No. 1, Diet No. 1, counts as essentially a separate person than Diet No. 2 for that same individual.

DR. PORTIER: But you're sampling the day's diet.

MR. MILLER: Yes.

DR. PORTIER: For one of the two days by random draw.

MR. MILLER: Yes, yes.

DR. PORTIER: So that was the second part of my question. There is a random draw for diet as well as a random draw for pesticide residue.

MR. MILLER: Random draw. But the random draw for diet is connected to that individual. Well, actually, I'll talk about it a little bit more in my presentation.

DR. PORTIER: We talked about the violations issue. I wanted to raise that again. I think you want to look that the policy, at least try to collect some data on what percentage of violations are actually caught.

The PDP data is market basket from food stores. Does it include market places? Road-side buys? Anything like that?

DR. SMITH: PDP is primarily from food distribution centers. It's not at the grocery store in general. In some commodities, for example, some of the grains and I think maybe grains were taken from a earlier point in the distribution, the idea was to get it as close to the distribution as practical to be able to reproducibly over time go back

and resample.

DR. PORTIER: To follow up on that question we had a minute ago, I didn't understand the resampling scheme. If I resample a diet and the child gets two apples in one day, assuming apples may or may not be exposed to OPs. But I'm going to choose apple for the fun of it. Do the apples get two separate random draw residues independent of each other, or do the two apples get the same residue?

MR. MILLER: In the DEEM, what it does is it totals it over the day. So if your child has, the person you're drawing, has two apples in one day, they will, essentially, be combined in consumption of grams per kilogram. And then it will draw one random residue value for that.

DR. PORTIER: That basically assumes, I guess, the two apples have the same residue which is fine for me.

And there was a another statement you made, and this is my last question. When you looked at the population groups assesses and noted that the children one to two years old have the highest exposures of all these groups, I gather, because you did not show us, you did not do less than one year and you did not do the other groups. You are assuming that those other groups are not as high of an exposure; is that correct? Or did you actually do the less than one year olds?

DR. SMITH: We have done less than one and the exposure is less. Some -- I mean the possibilities are, you know, you can go in and adjust the years that you want to take. So there are a number of possibilities. And at different stages in the assessment, we've looked at other combinations. At this point, I cannot give you an assessment, say, for children one to six all inclusive. We have three to five broken out from one to two, and we have looked at less than on. We just haven't included it.

DR. PORTIER: And do you intend to include that in the final? We got several questions about that yesterday. And I'm trying to understand why it's not in here then.

DR. PERFETTI: I mean, basically, not just this analysis, but with a lot of them. One to two are the most highly exposed right down across the line. We could put zero to one in or all the other age groups, but it would always, be to our knowledge, and, Dave, I think you can agree with me, it's always the one to two because they have the largest consumption with respect to body weight. So they always are going to get quote the "highest exposure". So if you know that one to two are going to be the worse case, everything else, the exposure is going to be less.

DR. PORTIER: I guess you can assume I'm from Missouri. I

like to be shown. "Show me" is the basic tenet here.

DR. KENDALL: Thank you. Any further points of clarification? Dr. Zeise. Remember, Dr. Miller, we'll go forward and probably clear up a lot of these questions. The presentation is quite long so I didn't want to break in the middle, at least let people to have a chance. So points of clarification.

DR. ZEISE: Yes. I was, also, wondering what the teenager, the upper end might look like for teens. Just curious, looking through, they're conspicuously missing. And I also wondered in terms of thinking through what might be happening with the tail if you looked at the issue of using composite sampling. What that would do is you're smearing out and probably have more zeros, more cases of zero and then higher values and that the composite sampling is actually also doing some smoothing at that upper end.

DR. SMITH: Actually, we do have limited -- we do have information from single serving versus composite samples. PDP has looked at three different commodities: peach, pear and apples. And there is also an industry market basket study that was done on single-serving basis; although, they do not have a composite direct comparison to a composite.

At this point we do not see a lot -- maybe surprisingly -- a lot of

difference between the distribution in the PDP between the single serving and the composite.

DR. ZEISE: At that upper tail.

DR. KENDALL: Dr. Bull.

DR. BULL: Just a real quick clarification of Chris's. When you looked at the less than one year old, is that distribution more or less the same; or is the high end exposure still even more exaggerated? When you say "across the board," I was trying to figure out what across the board meant. Am I making myself clear?

DR. SMITH: I'm not sure I can give you correct answer on that.

DR. BULL: Well, you have a curve that describes the distribution of exposures in terms of MOEs, the fraction of the MOE. Is that slope of that curve similar in the less than ones as it is to the one and twos. I could see the extremes being more marked in that group.

DR. SMITH: That's a good point. And I haven't carefully looked at that. We do know that they are less exposed in terms of comparing the curve shapes, we haven't gotten to that. But that is a good point.

DR. KENDALL: Dr. Reed.

DR. REED: This is a quick clarification question. Because you didn't see a great difference in residue distribution between single-serving-size surveys and the composite samples, and that's the reason you didn't use single-serving-size data; is that correct?

DR. SMITH: Yes. Possibly another reason. That's part of it. And just the feeling that if we have this huge data base of composite samples, and to use the single serving, we're limiting ourself to one small segment of data. If it did not make a difference, the composite samples, it would be consistent kind of analysis. We feel that composite samples may be better suited for catch catching co-occurrence. Can't prove that; but that's our general sense of it. That would be another reason.

DR. REED: Thank you. The other short question is: There's mention about choice years of PDP data. The analysis seemed to indicate that maybe you don't need that many years of data. There's a mention in the document about correlating that or the concern for pest pressure. Have you gotten any chance to go back and sort of looking backwards to see if there's any past pressure situation in that the PDP data actually picked that up in terms of residue?

DR. SMITH: That's part of the analysis that led us to change the question somewhat because we have not completed that. We are

interested in whether we can pull that out. We don't know.

DR. KENDALL: Any further comments related to this stage of the presentation? Before we move to Mr. Miller, I'd like to welcome Ms. Marsh Mulkey, the Director of Office of Pesticide Programs. We appreciate you joining us again. Would you like to address the Panel?

DR. ADGATE: No thank you.

DR. KENDALL: Mr. Miller, are you ready to proceed?

MR. MILLER: Just to kind of go through quickly the outline of the presentation. I'll provide an introduction, background information. It will be a brief overview and recap of probabilistic techniques used in preliminary cumulative risk assessment, or PCRA. I'll then talk a little DEEM(FCID) versus DEEM(FCID)/Calendex. As Bill had mentioned, his talk was on DEEM(FCID). And all the FCID means is the new recipes, the new publicly available recipes and the new '94, '96, '98 data. Do a little talk about the difference between those two and how the one includes a time component.

I'll talk a little bit then about the time frame considerations. Why it's important. There will be more details relating to this tomorrow. Specifically, how to compare these with a tox endpoint.

Then talk about modes in which Calendex can be used for a cumulative risk assessment which goes directly to the time frame

consideration issue. Consecutive daily estimates is one potential mode. That was the mode that was used in the preliminary cumulative risk assessment, PCRA, that provides separate estimates for January 1, January 2, January 3, et cetera. And alternative, methodology, which is available in DEEM which was not used for the December 3 document was rowing or sliding assume time frame approach. Again, there will be a little bit of discussion of this in terms of interpretation on this on Thursday.

And then going to strengths and limitation of these modes and the associated issues. This will include a comparison of some runs we've done comparing the 1-day assessment with the 7-, 14- and 21-day rolling averages. And you'll see those numbers here.

And then, finally, the questions for the SAP.

Just some points to remember, the presentation will not extensively review the step-by-step mechanics of DEEM(FDIC) Calendex algorithms. DEEM Calendex was reviewed in previous SAPs. However, I will try to give you a flavor of what's happening. And where it's important, I'll go into the details and differences between the modes.

The main presentation, here, concentrates on exposures through food. However, the principles apply to all routes. And, finally, I'll

remind you that no decision has been made on an appropriate MOE or threshold percentile for regulation.

When I talk about X-percentile graphs, they are meant to be illustrative only, intended to illustrate the concept. It's not that we've made a decision or are leaning toward any specific percentile or MOE.

Just some background, DEEM(FCID)/Calendex provides probabilistic assessment of exposures through food, water, and residential pathways. DEEM(FCID)/Calendex incorporates the concept of a calendar to aggregate or accumulate exposures -- it's a time-based approach -- which allows us to look at individual days of the year. Importantly, the approach allows appropriate temporal matching of exposures through food, drinking water, and residential pathways.

These temporal aspects are important for OPs to the expected seasonal use patterns. For example, it would be important to match springtime exposures from one applications through exposures through drinking water associated with spring runoff. Likewise, it would also be important to preclude or appropriately discount nonsensical or low probability events, perhaps treatment of house for fleas during the wintertime in the northeast.

So this is what Calendex allows us to do. Thus Calendex uses

probabalistic techniques to appropriately combine exposures from the food, water, and residential pathways in a manner which incorporates probabilities of exposure, use and application practices, human activities patterns, et cetera. Importantly, it considers their associated seasonality and timing.

So we expect, for example, probabilities of exposure, one can input as a data for Calendex at maybe perhaps 6 percent of the individuals users of a pesticide, or the 15 percent of apricots contain residues. So the probabilities of exposures can be counted in that way.

Use and application practices can also be accounted for. If the label directions say apply in spring, then it will be applied in the spring as per Calendex. If the label directions say, for example, or if we know that 80 percent of the users apply it one time and 20 percent apply a second application 2 to 4 weeks after the first, that information can be incorporated as well.

It also incorporates human activity patters, time spent on lawn, for example, time spent inside, et cetera.

The result of the result of the Calendex analysis is a collection or distribution of aggregate exposures, that's food, residential and drinking water combined, for each day of the year for the relevant

region. These exposures can be plotted as a time lime or profile of population daily exposures for any given percentile in this distribution. This is illustrated on the next slide.

This is just a quick 3D graphic which kind of summarizes DEEM Calendex output in a compact form. You can see the vertical access is the exposure. That's plotted against a time line in the bottom of horizontal axis from zero or 1 to 365 days. And the depth is the percentile for any given percentile. In other words, what we can do is plot exposures as a time line against any given percentile.

The graph emphasizes an important point that a time line, time-based profile exists for any selected percentile. We've shown some specific ones here, 10, 30, 50, et cetera. For example, there's one at 99 here which goes on. It goes along there from January 1 to December 31. And what that does is it shows or plots out the 99th percentile exposures for each of the 365 days of the year. 99th percentile for January 1, 99th for January 2, et cetera.

The three 3D graph essentially summarizes output that's specifics to DEEM(FCID)/Calendex as opposed to DEEM(FCID) which Bill talked about. Again, you get the three-dimensional part because of the time component is added here.

DEEM(FCID) analysis assess exposure from food alone, as Bill

said, without respect to timing or seasonality issues. What it does is it randomly matches report food consumption by individual with residue data. There's no time component to this. The result, as Bill described, is a single distribution of exposures and a single value estimate of risk at any percentile of exposure.

How does DEEM(FCID)/Calendex, which incorporates the time component differ DEEM(FCID) when we do an aggregate or cumulative assessment in which pathways are combined, time and considerations become important? DEEM Calendex performs this analysis in a manner in which time considerations are incorporated. It does this by performing separate analyses for each day of the year. The result is 365 separate distributions of exposures for each day of the year. And exposures can be at any given percentile, 99th, 95th, et cetera, can be plotted as a time-based exposure profile.

These differences are summarized on the next slide. DEEM(FCID) considers food alone; whereas the DEEM(FCID)/Calendex considers all pathways, food, water, residential. Timing is not considered in DEEM(FCID). There's no day-to-day variation, whereas timing is considered in DEEM(FCID)/Calendex. There's some day-to-day variations in the diet. That will be explained a bit later in this presentation.

And another difference is single-exposure estimate is provided DEEM(FCID) at any given percentile; whereas, DEEM(FCID)/Calendex provides 365 sequential daily exposure estimates for any given percentile.

With that as background and the knowledge that DEEM(FCID)/Calendex can consider time, there are several issues to the SAP regarding time-frame considerations. Remember that exposure's only half the risk equation. It's important to consider how the estimated exposure is compared with the toxicity endpoint.

In the preliminary cumulative risk assessment, PCRA, toxicity endpoint is based on the BMD10 which reflects a multi-day dosing study or a series of multi-day dosing studies. And you heard about this yesterday from Anna and Woody. You, also, heard about it last September at the 2001 Scientific Advisory Panel meeting.

In the report you provided, there were two statements that cumulative risk assessment should ideally compare toxicity endpoint and exposure durations of the same time frame. And, also, to the extent possible, comparison should take into account the pattern of human exposure.

Again, you're scheduled to hear more about this comparison tomorrow under the risk characterization session. But in my talk here,

what we'll focus on is the time-frame issue and how it's handled by DEEM and Calendex.

DEEM Calendex program can perform analyses using a variety of time frames. You heard from Bill the single day. This presentation considers two specific modes of analysis which are available in Calendex. One is the single consecutive daily estimates, January 1, January 2, et cetera. That was the analysis that was used in the PCRA.

The second is a rolling or time-frame approach where it takes a rolling average, considering, for example, January 1 through 7, then January 2 through 8, then 3 through 9, et cetera. It provides an average exposure over that time period.

I'll emphasize that the examples I'll give you here are illustrative only, intended to illustrate the concept. The numbers are not real. And PCRA used, again, the first option; the single-consecutive day rolling estimate not the rolling time frame. Although at the end of this presentation, you'll see those results for the rolling time frame and be able to compare the two.

Just first option, the single-consecutive-day analysis, the analysis we used in the December 3 assessment, provides separate independent exposure and risk estimates made for each day of the year. And I'll show this in the next few slides, summarize how that is

done.

The estimates, then, are arrayed chronologically into an exposure time line for any selected percentile and graphed. These represent independent daily estimates of risk on each day of the year. Importantly, they're not necessarily -- as you'll see in the following slides, they're not necessarily the same individual on consecutive days. What I mean by that is the next several slides show how this is done by DEEM Calendex.

So for a single-consecutive-day analysis, the analysis that was done in the assessment, and, again, the numbers here are not necessarily -- they're not necessarily the numbers. It's illustrative only. What DEEM would do would begin with January 1. DEEM(FCID)/Calendex begin with January 1, CSFII, Individual No. 1.

What DEEM Calendex would do would then estimate the exposure and plot that exposure to the individual on the histogram. So that could come across as -- essentially think of it as a first block of a histogram would be located someplace along there.

How is that exposures estimated? It's done for that Individual No. 1 on January 1. It's done by randomly choosing one of Individual No. 1's self-reported diets and then randomly selecting a residue for

each component of that diet. And that is essentially summing them up and estimating an exposure based on that.

And the same thing would be done with Individual No. 2. And that would work out -- actually, if you could back up for a second. That would be the same thing would be done for Individual No. 2. And the result is a slowly build up essentially a distribution which might look something this, a histogram with a shape that looks something like that.

In this case then what we do is, if we were choosing to plot out the 99.9th percentile, what we would do is estimate what that is. In this case, it might be individual No. 10,456 that would plot out at the 99.9th percentile and essentially estimate the exposure from that individual at that percentile. That might, for example, translate to a MOE of 84.

We than move on to January 2 and do the same thing. Starting with Individual No. 1, estimating the exposure and plotting. And, again, we do it for all the individuals. Individual No. 1, 2, 3, et cetera.

In this case, these would be plotted out for all the individuals. In this case, the 99.9th percentile individual exposure might be Individual No. 1,492. We estimate exposure. And that might work

out to be, for example, an MOE, margin of exposure, of 92.

We would proceed through each day of the year in this through December 31, which is here. In which case of the 99.9th percentile individual or exposure, might be Individual No. 18,912. again, we'd estimate an MOE with that exposure.

The net result of this is we end up with 356 different 99.9th percentile values. Again, what we've done is for each day of the year we've run through each individual and we can pick out the 365th -- the 99.9th percentile values.

What we do is take each of these 365 99.9th percentile values and then plot them out for each day of the year, January 1 through December 31, that population percentile. The resulting time-based exposure profile represents, in this case 99.9th percentile exposure for each day of the year.

It's important to remember that each day of the year is considered independently. It is not the same individual. If you remember on January 1, it was Individual No. 10,456 that was at the 99.9th percentile. On January 2, it was a different individual.

One can see this plot on the next slide here. The vertical axis. These plots are central to the understanding and interpreting the cumulative risk assessment. I'll go through it in some detail.

Remember, this is the single day assessment as we used in the preliminary assessment.

This is the vertical axis here. It's the exposure. Here is the time line. The horizontal axis is the day of year from January 1 through December 31.

Continuing with the example, if you remember, January 1, the 99.9th percentile exposure value was associated with Individual No. 10,456. He had an MOE of 84. So that would be plotted here for January 1.

For January 2, the 99.9th percentile individual, the value associated with the 99.9th percentile exposure would also be plotted. In this case it might be an MOE of 92. It continues through the year through December 31.

Just some key points. These are all, again, each different individuals. These are also one-day exposures.

How is this interpreted, for example? Day, for example, if you wanted to interpret the MOE associated with Day 31, this would essentially look up here, and this would be perhaps an MOE of 58.

How is that interpreted? On Day 31, the day we were looking at, on the next slide, the MOE for food, the interpretation would be the MOE for food at the 99.9th percentile would be 58. The

translation of that would be the exposure to the 99.9th percentile individual on Day 31 is 58 times lower than the BMD10.

Day 32, it may be that the MOE was estimated as 66. The translation of that would be that the exposure to the 99.9th percentile individual on that day is 66 times lower than the POD. Remember, it's very likely that that is a different individual than the 99.9th percentile individual on January 31. Just as on January, the 99.9th percentile individual was different from the individual on January 2.

The next slide shows some pros and cons of this method. This was the method that was used in the PCRA. It's easier to identify risk contributors and sort them out using the CEC function of DEEM. That's the function that Bill had talked about some.

It's also health protective from a multi-day standpoint. When one looks at a sustained or extended period of time of elevated exposures, it's unlikely to be the same individual that's being exposed.

However, there are a number of disadvantages to this. One is that the point of departure, the BMD10, is based on multi-day exposures. The animals, if you remember from yesterday, are dosed daily for an extended period of time to estimate the BMD10. It might of be of concern would be the relevance of comparing a series of elevated single-day exposures to a multi-day endpoint.

Another disadvantage is the second consecutive daily estimates are likely to over estimate multi-day exposures to an individual at the higher percentiles. For example, it's not possible to interpret an extended serious of elevated exposures on consecutive days as representing extended period of exposure to the same individual. In other words, we haven't strung together consecutive days for the same individual. So the individuals are different.

If we were to string together consecutive days for the same individual, what we'd get from DEEM we'll be able to have essentially a rolling time frame approach. And this is what this next series of slides considers. And I'll talk about stringing the days together and go through a detailed example of how this is done.

It can, also, be looked at as essentially a multiple sequential day option. In this rolling-time-frame option, a rolling average exposure is calculated over multiple days for each individual. For example, January 1 through 7, then January 2 through 8, and January 3 through 9, et cetera.

It's this series of multi-day average exposures that then serves at a basis of comparison with the BMD10 -- with the POD. More, specifically, this distribution of individual-based multi-day average exposures is compared with a multi-day BMD10.

The next slide show an example of this. And, again, the numbers are not real but are meant to be illustrative only.

Specifically, this specific example will deal with a 7-day rolling average. It begins with individual No. 1 on January 1. And you can see this is going to be this January 1 through 7 rolling average. This exposure to this individual on January 1 is estimated from this DEEM Calendex software as .012 milligrams per kilogram per day. That's estimated, as always, by randomly choosing CSFII Individual No. 1, Day No. 1 or Day No. 2 diet; randomly choosing residues associated with each component of that diet; combining those; and summing them over all foods reported consumed by that individual on that day. So that point .012 is estimated in that way.

The same thing is done for that individual for January 2, again, choosing one of his two randomly reported diets. And January 3, et cetera, all the way through through January 7. You can see on January 2, the estimated exposure using that is about a little bit over .006.

The next step after that, after we've calculated exposure from each of those days is to calculate an average exposure over the entire full 7 days. Here the average exposure, you can see, is about .006 milligrams per kilogram.

We've done this then for Individual No. 1 for January 1 through

7. We now move on to Individual No. 2 for this same time frame. Again, starting with January 1, estimating the exposure as before for each day, January 1 through January 7. After that's done, we calculate a 7-day average over this time period. Here you can see it works out to be about .007 milligrams per kilogram.

We continue this through all individuals in the survey, calculating it for January 1 through 7. If there were 15,243 individuals in the survey, for example for the last individual, the 7-day average exposure works outs to be .005 milligrams per kilogram.

If there were 15,243 individuals in the survey, we'd end up with 15,243 7-day average exposures for January 1 through 7. Then what we would do is sort them from high to low and pick out this 99.9th percentile exposure and plot this value for January 7.

So what we've done is for January 1 through 7, calculated for each individual a rolling average and picked out the 99.9th percentile values in this case just as an example.

For the next rolling time frame is January 2 through 8, we go back to Individual No. 1 and calculate exposures for each of the days, January 2 through 8, again randomly choosing each day one of his two reported diets and combining it with a randomly selected residue. We do the same with Individual No. 2, Individual No. 3, et cetera, for

January 2 through 8. Continue all the way through and then slide along and do 3 through 9, January 4 through 10, et cetera, until we get to this last individual which would be January 1 through 6. It rolls around. We'd end up with 365 different 99.9th percentile 7-day rolling average exposures and plot them over time as we did before.

There are a number of advantages and disadvantages to this approach. One advantage is that it incorporates the variability in exposure for an individual across multiple days. This multi-day average exposure may be the actual exposure of interest to compare with a multi-day endpoint.

It's also likely to provide a more realistic estimate of exposures across multiple days. And, again, if it's not a series of single-day exposures we're interested in, this allows us to calculate high end multi-day average.

It's also flexible with respect to matching time frames associated with the POD. One can chose, for example, this example was 7 days. But one could chose 7-, 14-, 21-, or 28-day rolling averages.

There are a number of disadvantages, too, to this approach. Break down into two basic areas, one associated with food consumption and the other associated with residue. UDSA, CSFII

does not provide consumption data across the multiple consecutive days which would be of interest. It's limited to two days of records of reported intake. Also, those two days are not consecutive. They are 3 to 10 days apart.

As a result, the multi-day average exposure for any individual uses only two days of reported consumption data for that individual. With the rolling average approach, what we're using is those two days of reported intakes to simulate 7 or more days of eating. It repeats these randomly throughout the time frame of interest.

The other aspect concerns food residues. There are no longitude and residue data available. For example, if I ate a star fruit yesterday and star fruit today, if they came from the same Safeway, they're likely to have the same residues than if the one I ate yesterday was from Safeway and the one I ate today was in the company cafeteria. So there's no longitudinal basis on residues for that.

Just more specifically on those two points regarding, first, on food consumption aspect. Any consecutive day period of interest for an individual will contain a series of repeated diets which would tend to underestimate the variability. This will tend to over state potential exposure at the upper tails of this distribution to the extent that reported food choices or diets are associated with higher exposure.

On the aspect of the residues, the second aspect I talked about more specifically. Since residue values are anew at random, for each day during the time frame of two occurring on subsequent days, may not be accurately reflected understate potential at the upper times. If an individual exposure is associated with pesticide residue, two examples, one might be juice you drink from this morning, may very well be the very same one you drink from tomorrow morning. And it will have the exact same residue concentration. In DEEM(FCID)/Calendex, a brand new residue was selected for that second day.

Similar situation is bags of produce. The produce I eat today may very well be from the same bag I eat tomorrow. They likely share the same treatment history.

If the rolling time frame average in DEEM is selected, it allows -- the example I gave was 7 days. But it allows the user to choose various time frames. We've redone the analysis using a 7-, a 14-, and 21-day time frames. And you'll see these in the next graphs.

Increases, two things you'll note as you go through these. And, again, you'll note when the next graphs are shown. But increases in time frame, going from 1 to 7 to 14 to 21 over which the averaging is performed, results in two main things. One is the attenuation of

variability; and this other is an increase in the MOE, essentially, a decrease in the exposure.

You'll see that in the next two slides. Keep in mind that it's a reverse log scale. And, also, the degree to which these changes occur are dependent upon the selected percentile. The effect seems to be greater at higher and more pronounced at higher percentiles than at lower percentile.

These are shown in this slide here. The very top one, the sky blue one, is the one day. What we did in the assessment using the one day time period. The next three underneath that are 7-, 14-, and 21-day time periods.

So, again. These are averaging exposures. You note the attenuation goes down as you go from the one day here, the sky blue down here, less variability. And the there's a decrease in the MOE. You're averaging additional days into it, so there's an increase in the MOE, a decrease in the exposures.

This is actually -- this is an example of this higher percentile example where the effects were more pronounced. At the lower percentile example, you can see the same thing except the effects are less pronounced. Again, the sky blue is the one day; and it looks like the 7, 14, and 21 are almost coinciding, but they're very close.

I guess a series of questions would be the next set.

DR. KENDALL: Think I'd like you to have you stop there because we'd like to have some clarification from the Panel. Then we will take a break and come back with the public comment period. After that, I'll have you read the questions. And then we'll begin the deliberations.

At this point, any clarification questions from the panel? Dr. Durkin.

DR. DURKIN: I have three quick things and it may be a lack of understanding here. You indicated that Calendex makes assumptions about when the chemical is applied. So if the label said it's applied in the spring, that enters into it in some way.

MR. MILLER: That is entered into it in the residential side of the assessment.

DR. DURKIN: Only the residential. Okay. That's fine. We'll move on.

You showed some 3D graphs. If we asked for a 3D graph of the day of the year, the percentile, and then on Z axis the chemical, would that be possible? Can you spit those out?

MR. MILLER: If you were looking at a specific chemical.

DR. DURKIN: No. An array of different chemicals. It gets

back to my previous question about can we track these by chemical. I guess that's what I'm trying to nail down real clearly here. It seems like you could do it from the food, the Calendex.

DR. SMITH: We think we can do that. It would be a lot manual.

DR. DURKIN: So it's not easily done.

DR. SMITH: It would require kind of a multi-step process.

DR. DURKIN: It wouldn't just spit it out. Okay.

And then the last item is really just a follow-up on a question that Natalie had. In any of these residues is home grown vegetation considered?

DR. SMITH: No.

DR. DURKIN: Okay. Thank you.

DR. KENDALL: Any further questions?

DR. RHOMBERG: On the residential exposure component, I assume, does that take into account some kind of attenuation of exposures over time in ways that are modeled according to residential?

MR. MILLER: Yes. Jeff Evans will be talking about that later today. But it does. If you applied that three days ago, it would attenuate that over the three day up to today.

DR. RHOMBERG: You made a big point of saying they were

not real numbers for the rolling average. Was any of this real at any place? In that when these last graphs that you showed with the rolling averages, were those based actually on doing the exercise that you had described earlier?

MR. MILLER: Yes, yes. The point I wanted to make on the real numbers is that, when I was showing the average, the rolling time average, the Excel graphs from 0 to .014. Those real numbers there. We didn't go back and look at Individual -- that's good. We didn't go back. We didn't go back and look at Individual No. 1,492 plot out his exposures for example. There was some confusion about that at the technical briefing.

DR. RHOMBERG: Okay.

DR. MILLER: So I wanted to make it clear.

DR. RHOMBERG: And since you only have two days of diet for each person, you are sort of flipping back --

MR. MILLER: Flipping back and forth, yes, over those seven days.

DR. RHOMBERG: Randomly, you could pick the same diet twice in row if it happened.

MR. MILLER: Yes.

DR. RHOMBERG: And when you come up with different

values, that's because --

MR. MILLER: Different residues.

DR. RHOMBERG: -- of different residues.

MR. MILLER: Yes.

DR. RHOMBERG: Okay. Thank you.

DR. KENDALL: Further questions? Dr. Portier.

DR. PORTIER: In essence on the flipping diet issue, you actually flipped the diets for 365 days for an individual, don't you, because the 1 to 7 is the same individual for 2 to 6.

MR. MILLER: Yes.

DR. PORTIER: And then you and 2 to 7 and then you add the 8. So the diet is flipped completely.

MR. MILLER: Yeah. But it's always connected to the same individual.

DR. PORTIER: Just so I'm really comfortable, I want you to reassure me again that the graphs that you show with the rolling time frames approach, the examples are clearly not OPs since those numbers are only 10 away from the BMD. Not the later graphs, but the early single rolling time frame graphs.

MR. MILLER: Yes, yes.

DR. PORTIER: I want to be certain.

MR. MILLER: Yes. Those are not.

DR. PORTIER: The couple of questions I had about some of the statements you made in -- 1, 2, 3 further graphs down from that one -- you have pros and cons for rolling-average-based estimates. There.

The second point. Why? I'm not sure I understand this. Clearly, the assumptions that go into the analysis are violated; there's absolutely no doubt about that. The double diet back and forth is clearly not a realistic diet. The residues selected independently from day-to-day without any correlation structure is clearly going to be violated especially into details of the distribution. Why do you believe this is more likely?

MR. MILLER: Which specific slide and which specific point?

DR. PORTIER: It's this slide, Point No. 2.

MR. MILLER: Okay. Why do we believe it's likely to provide a more realistic estimate of exposures across multiple days?

DR. PORTIER: Yes.

MR. MILLER: If you're interested in a multiple-day time frame, we believe that it provides -- the alternative, the one-day time frame -- let me take a look.

DR. PERFETTI: Dr. Portier, in my own simple way. The way I

look at it is, if you do this day by day, you're picking an individual, say, at the 99.9th percentile one day and you're picking that individual at that percentile is unlikely to be at that percentile on a following day. Whereas for this day by day, you got a different individual each time.

I mean if you get exceptionally bad day on one day, the chances that you're going to have an exceptionally bad day for the next seven days are rather low.

DR. PORTIER: But the question here, I guess, I'm interpreting maybe differently than what you're saying. I'm thinking about distributions. So I got a distribution for single-day exposures. And then there's a distribution for multiple-day exposure. And the way I read this is that you're arguing that the distribution seen here for this procedure is more likely to be correct if you're interested in truly multiple days --

MR. MILLER: It's multiple days, yes.

DR. PORTIER: -- than is the distribution for single exposures. And I'm not convinced of that. I was trying to give you an opportunity to convince me that the two assumptions that are violated don't simply drive us regression to the mean, which is why we might see reduced variability, why we'd see lower tail behavior, and to get some question

-- have you done alternatives? There are some obvious alternatives. Don't use the two days back and forth. Choose random days and bring them together, find some correlation structure from day-to-day sampling, and use that.

Have you done any of that, some of the things we discussed when Calendex came up?

MR. MILLER: Yeah. We've talked about that one. One possibility is to hold the day constant -- hold the diet constant throughout the seven days, don't randomly bounce back and forth. Another possibility would be to choose different residues -- keep the same residues, for example, and find out how much of an effect that has.

We haven't gone ahead and done any of those analyses at this point. We're looking for recommendations and thoughts from you on how that might be applied.

DR. PORTIER: And let's see if I had any other questions. Yeah. Two more slides down I'm trying to understand this conclusion as well. Could you repeat the explanation for me.

MR. MILLER: Any I'll just read the slide first and then go through it. Any consecutive day period of interest for an individual will contain a series of repeated diets which tend to underestimate

variability. So, for example, if we're repeating, if an individual has reported --

DR. PORTIER: That I got. It's the next one.

MR. MILLER: Okay. This will tend to overstate potential exposure at the upper tails of the distribution to the extent that reported diets are associated with higher exposure. So for example, if I consumed, for example, two ginkgo fruits over these two days -- and that's an unusual event -- I'm going to repeat consuming those ginkgo fruits through all seven days.

So it's kind of -- in reality over seven days, I wouldn't be eating those on all seven days. But it's artificially repeating that consumption pattern over the seven days.

So if to the extent that the diet is responsible for high residues, the choice of the diet, the food choices, that would have a tendency to overstate the potential exposures.

DR. PORTIER: Okay. I guess I understand that point now. And by overstate, you mean overstate to some true distribution that we really don't know.

MR. MILLER: Yes, yes. And that's just at the higher percentiles. It would be kind of a regression to the means. As you add more variety to the diets -- instead of repeating the two diets over

and over again, if you're high, you would tend to move lower.

DR. PORTIER: And in the food consumption survey, were all diets two days?

MR. MILLER: All the diets -- okay. There were -- they asked everybody for two days and the data that we use in DEEM is only those individuals that reported the full two-days worth of consumption.

DR. PORTIER: So the individual-day diets are derived from the two-day diets absolutely guaranteed.

MR. MILLER: Yes.

DR. PORTIER: Thanks.

DR. KENDALL: Any further points of clarification? Mr. Miller, I thank you for an excellent presentation. We'll break at this point for 15 minutes. We will reconvene for the public comments. And then we will move into the panel discussion. Thank you.

[Break.]

DR. KENDALL: If everyone with take their seats, we'll reconvene. Okay, this are reconvene. We're in the public comment period now. We have had two individuals registered to speak. The first I would like invite to the table Ms. Ingrid Kelly of Bayer Corporation. If you would approach the public commentor position

over there. The microphone is available. Please state your name and affiliation for the record.

DR. KELLEY: I'm Ingrid Kelley, Bayer Corporation.

I'm here today on behalf of the Implementation Working Group to talk a little bit about their comments on the OP cumulative risk assessment, especially the food exposure part of it.

First of all, IWG commends the Agency for doing such a wonderful job in their move forward toward producing a cumulative risk assessment, which is, as you all know, a tremendous job. The IWG recognizes the difficulties involved and we want to be sure to acknowledge that we believe that the Agency is on the right track. There are many, many improvements that can be made that we can see, and we would like to advance some of them here.

We feel that, as I said, we are on the right track. But the OP-CRA process and methodology is precedent-setting technology and methodology all of the other chemicals will be evaluated with a similar technology. That's why we feel, as Marsha Mulkey put it, it we need to put in the best and sound science. Science must be the basis for this risk assessment.

Transparency and understanding are equally important. Because if we don't have that, we don't really understand the science.

Stakeholder input is equally important because each of us have our own little niche and we must be sure to listen to all the opinions and stakeholders, including the growers who have a particular interest in this risk assessment.

So we hope and, therefore, that the Agency will continue to improve this assessment; and, finally, will give us another opportunity to comment. In other words, we are hoping the Agency will produce an interim cumulative risk assessment where we will have the opportunity to see what the improvements might have done and how further we can improve this assessment.

I have to put my glasses on. IWG believes that the accuracy and realistic assumptions for the dietary data inputs are extremely important in the cumulative risk assessment, as well as single risk assessments. The assessment is, if it is peppered with overly conservative assumptions, often is taken as protective would then would mask the real risk drivers. Therefore, we have to be sure and not be overly conservative in our assessments then we want to find real risk drivers.

I have, myself, found this to be the case with individual assessments. I have some proof of this that conservatism can, in fact, lead you to the wrong direction.

And with this in mind, we hope that the Agency, as they have indicated, will further refine the risk assessment. We hope that they will consider the following considerations. Perhaps they might reevaluate the blended and nonblended issues.

Part of the reason for that is because the new DEEM(FCID) does include new recipes, new food groups, that have never been there before. They should be evaluated whether or not an item is blended or nonblended. This makes a big difference in the risk assessment.

Processing information is plentiful. The Agency has at its disposal the processing information from industry; it has, also, at least 40 years literature around the world that has been produced by scientists in universities that show that OPs, especially, degrade when they are processed in homes by cooking and baking and other processing.

We are applauding the Agency for using registered and supported users only in the risk assessment. These are, after all, the only thing that the Agency or industry can do anything about. All of rest of it that might be illegal use should fall into a separate category.

We believe that the Agency should adjust the PDP data to reflect only current use patterns. In the lease 10 years, many companies, including my own, have come up with different and

competitive chemicals to OPs. These have already replaced many OPs. And the 1994-1995 PDP data does not reflect this. I, again, have from my own company several instances where this is the case. I will forward those to the Agency, and they may share them with you as they wish.

Also, there is the OP market basket survey which was conducted on I believe 10 or 13 -- I'm not entirely sure -- commodities on single servings. This data is in the hands of the Agency. They have evaluated it, and we believe that it could be used appropriately.

We believe that the incremental changes taken collectively will improve the overall credibility of the OP-CRA. We also believe that in refining the assessment, the Agency will have a better tool for more reliable decision-making.

The stakeholders need to have opportunity and access to the EPA's CRA tools and data. As I have mentioned, the Agency has used the new DEEM-Calendex. None of our colleagues in our industry have access to this data base or this model. We have not had a chance to evaluate it. The versions that are out now have not been peer reviewed, even though older versions have been.

The new translations of recipes incorporate new food forms that include baby food. We are not familiar with those food forms. We

have not really had a chance to get an input on that.

Also, these new translations -- and I don't understand how -- and this is where, perhaps, transparency gets lots. The new translations in some way incorporate into the new recipes processing factors, I was informed; and this is something where we need some clarification. Because whatever processing factors we might give the agency, they may not able to use but we won't know why. So we need to have some review state to find out what went on there.

Also, new PDP data have been used. We congratulate the Agency for working with USDA so closely to obtain this newest data. We are very glad for that. But the registrants and the stakeholders have not had a chance to see the data as yet. It just came out, I believe, last week publicly.

We, also, believe that it is useful, and the Agency did indicate, which we're glad for, that they will do analyses using the CARES and other software. We believe that is essential. Sometimes the different model will point out different problems in data sets or things that are important that have not shown up in one particular model because they have not been anticipated.

Finally, the IWG supports the rolling time frame average for the dietary CRA and the whole risk assessment. Partially, if the Agency is

going to use the BMD10 based on a 21-day toxicology value, it kind of would match the hazard, the acetacholinesterase inhibition at steady state with the duration of exposure. We believe that this makes sense.

Also, Jeff Driver will later on, for the nondietary portion, inform you why there is also good reason why this makes sense for nondietary considerations.

UDSA Food Survey Research Group should be consulted on related food consumption issues as you have discussed when David gave his talk. There is, for the food consumption, only one- and two-day period for each individual that information was gathered. And it was not in consecutive days.

However, the UDSA, have older data bases that do is consecutive information. And this could be used to correlate consumption patterns. And in addition to that, ENHANES (ph) might be able to relate some of these food consumption patterns and see what is the best way to handle this particular data.

Our final recommendations from the IWG is that EPA should reissue or issue a revised or interim OP-CRA that has inaccuracies and improvements included in it. Hopefully, by then, there might be a comparison also and an analysis of the outcomes of alternative models, the Calendex and CARES and the Lifeline. I think we can learn from

all of them.

We have to, also, evaluate the alternatives in methodologies as David has pointed out. I think the Agency is doing a good job in doing that. And I think they're going to go further on that. We appreciate it.

And, finally, we do hope and we do encourage the Agency to allow sufficient time for additional peer review and public comment before finalizing the OP-CRA. It is an important tool for now and for the future. Thank you.

DR. KENDALL: Thank you. Any questions from the Panel for Ms. Kelly. Thank you very much. The next public presenter that's registered is Dr. Judith Schreiber, New York State Office of the Attorney General.

DR. SCHREIBER: Good morning. My name is Judith Schreiber. I'm a research toxicologist in the Office of the Attorney General of New York State and a Senior Public Health Official there.

I have a number of comments, mostly clarifications, of what was discussed this morning. I didn't bring any prepared comments with me today. These are all really just questions of clarification. But my office will be submitted comments, written comments, to the docket.

We certainly thank the EPA and SAP for undertaking such a

broad and comprehensive and very needed assessment on OPs.

That said, the hotel actually provided me with this apple as prop which was very nice. Just one comment regarding the ginkgo fruits and how many times you might eat them in a row. I would just point out it's much more likely that a family is going to buy a bag of apples and eat those apples over the course of a week, perhaps one time a day.

That's not an unreasonable assumption. I just wanted to point that out. My family eats a lot of apples. And I think children in general eat a lot of apples and apple products.

I was very concerned about the decision by the EPA of not including violative and nonregistered use residues in the exposure assessment. Of course, what goes into that model is very key about what kind of numbers you generate coming out.

I was interested in whether the EPA has conducted or whether the SAP had requested the EPA to conduct a sensitivity analysis of, for example, using those violative residue data and looking at how the assessment would differ. I think that's really very critical.

I don't know. Maybe someone on the SAP can inform me whether that was something that was requested or has EPA ever looked at that? Anybody?

MS. MULKEY: Why don't we hear all the questions, and we'll try to address them just as we have tried with other public commentors.

DR. KENDALL: Very well. We'll try to summarize a response at the conclusion of your presentation.

DR. SCHREIBER: All right. I'd just like to emphasize that it seems to me would be just like having a high school student grade point average that we decide not to include his flunking grades, his failing scores, because he wasn't supposed to fail and so we're only going to include the passing scores to figure out these averages.

It just doesn't seem to make sense to me to exclude what we know as, we do have a lot of data, that indicate that there are residues on foods for which there is no tolerance for various OPs. Why not include those if in fact they turn up time and time again.

I had asked this question once before at one of the KARAT meetings, and I was told that the data is so robust, that it wouldn't make any difference. Well, if that's true, I'd like to see that analysis. I think it would be very important for both U.S. and imported products for those.

One thing that I'm not sure this is the appropriate time for it. But the MOEs have come up quite a bit through this morning's

discussion. Has the EPA or the SAP considered what is the appropriate margin of exposure for the cumulative risk assessment? And I understand, at least in part from this morning's discussion, that that is something that EPA is not ready to is decide at this point.

If that's true, I think the risk assessment is missing the punch line, is missing the risk management part. And I think it would be very hard for public commentors to make any final determination on this risk assessment without that component. So I think that really is very necessary and perhaps either the EPA or the SAP can elaborate on what is the margin of exposure that is going to be considered to be sufficient under the FQPA for cumulative risks for OPs.

In following the previous commentor, I, also, do agree that if there is going to be substantial changes or elaborations of these kinds of points in the final risk assessment, that you public be allowed to comment once move before the document is finalized.

And one other point. I believe it was mentioned that the children age one to two are the most highly exposed population. And I was wondering, also, whether for the younger children from zero to one year olds is exposure through breast milk and contaminated formula included in the assessment in the OPs? Perhaps somebody could address that.

That concludes my informal comments. And as I mentioned, we will be providing written comments to the EPA on this document. Thank you very much.

DR. KENDALL: Thank you. Ms. Mulkey.

MS. MULKEY: This might be as good a time as any to say a little bit more about the violative and also talk about the canceled and phased-out products. And then I'll ask our scientists. We have had this question about breast milk and the water in formula and so forth. So I'll ask them to go ahead and do that, and that will wrap this piece up if that makes sense to you guys.

DR. KENDALL: Yes.

MS. MULKEY: Since it is the same topic that we're in the middle of anyway.

DR. KENDALL: Absolutely.

MS. MULKEY: I explained a little bit of the policy thinking behind the way we have addressed violations in other context. But with regard to this particular data set where you have in the PDP data residue levels that are above the tolerance, I understand that Dr. Miller did give some data this morning about the frequency and the extent of those data in the data set.

And I think that is a situation which we've been very mindful of

trying to understand the science implications of that policy choice. And I don't want to leave the impression that we are uninterested in that. That is why we developed the information about the extent to which we're seeing it and so forth. So I don't think I have anything more to say about that other than that's what led to our having the information we offered earlier about the extent of that situation.

The other is something that also came up in public comment yesterday and the Dr. Portier asked us to speak to which is the chemical crop combinations. In some cases, it's whole chemicals; in some cases it's chemicals and some uses as to which we have taken regulatory action as part of the individual chemical risk assessment process and/or where the companies have voluntarily changed their registrations materially whether for risk-regarded reasons or otherwise.

And we do have -- we have done that with regard to a number of OPs and their uses. And in most cases, as is typical for a practical way of ending a use, there is some kind of time line. Even when there is a immediate cessation of the sale of the product, there is a period of clearing the channels of commerce. Even after there is a period beyond which there is now allowed use, there is a period for treated foods, for example, to clear the channels of commerce.

So we are in the glide path for a fair amount of risk reduction. I've looked at the dates, and it would take a while to read all the dates. But sort of the last dates in the list are not, at this point, five more years from now. Most of them end the at the end of '02 or '03. There are some residential uses that go into -- there's one that goes to the end of '05. But even that, of course, is less than four years from now.

Our thinking on this was simply that the risk management choices had been made and that they were on a path of either such expedition as that you couldn't practically make a lot of difference in that or reasonable expedition; and that since risk assessments are conducted among other reasons for the purpose of risk management, that including these in the risk assessment would not materially improve our risk management decision-making. So that's the thinking behind that.

Almost all of the direct food uses have end sale dates or end use dates by the end of this year, especially those on fruits and vegetable. A few go into '03. That gives you a general answer. That information is all available on our web site, but I won't read through each one. If there is interest in a particular one, of course, we could speak to it.

And now maybe Dr. Smith can address the formula and breast milk issues.

DR. SMITH: With respect to children less than a year old, or for that matter any of them, the potential for contamination of formula is covered to the extent that the survey would adequately reflect what they ate.

What is not in the survey is beast milk, the mother's breast milk. It is our best judgment that that is not a significant oversight on our part. The evidence that we see indicates that there's not much potential of OPs in mammalian milk. We are including cow's milk, of course. And there are no OP residues accumulating in those.

So, basically, that's all I would say on that. It's not included, but it's our opinion that that is not a major oversight.

DR. KENDALL: Any points the Panel wishes to make or ask EPA? Dr. Bull.

DR. BULL: I have a little bit of concern, and I'm going to ask this question kind of publicly. The issues related to the cumulative risk assessment and there's issues that go to OP's regulatory mandate. I'm trying to figure out, if we're really, truly interested in cumulative risk assessment, where you would have to bring in some of these other less frequent contributors to OPP exposure but recognize at the same time if you do bring those in you have to realize that you can't address many of those extreme exposure through your regulatory mandate. It

probably goes to other places within the Agency or perhaps, or probably in a lot of cases, to other agencies.

So I'm trying to figure out when we're talking about a cumulative risk assessment, are we really talking about a cumulative risk assessment or are we just talking about a cumulative risk assessment that deals with what's in OPP purview?

MS. MULKEY: We are not limited to what is within our purview. I didn't mean to leave that impression. We do not, in the OP risk assessment, other than some drinking-water-related considerations, most of the exposure sources do happen to be within our program. But I didn't mean to leave the impression that that was an inherent element of our approach.

DR. KENDALL: Any other points from the Panel? Are there any other persons who would like approach the Panel for public comment? With none, we will close the public comment period.

I would like now to have Dr. Smith and Miller to go ahead and present the questions to the SAP, and we'll move forward.

DR. SMITH: Question one for food. In the preliminary OP cumulative risk assessment OPP used all available PDP monitoring data generated since 1994 as the basis for the residue distributions of pesticides in treated foods. As a result, some foods multiple years of

data (as many as five), while others have only a single year of data. All years of data were included to provide the most robust data set possible. These data were extended to cover foods and processed forms of foods for which data are not directly available. Additionally, some other foods were included in the analysis based on other less robust data from FDA.

OPP is conducting a sensitivity analysis in which the residue contributions from specific foods, either one at a time or in combination with other foods, are removed from the analysis. This analysis is being conducted as part of the effort to determine the contributions of specific commodities and chemicals to the upper tail of the exposure distribution. And some of the preliminary results are shown in Table 1 of the addendum which was supplied to the Panel.

Partly as a result of this exercise, OPP has observed -- can I just toss in, too -- that, also, it was shown on the slides in my presentation in a slightly different forms for the sake of other people here.

Partly as a result of this exercise, OPP has observed that the more variables, that is, commodities, chemicals, years of data, that are included in the exposure distribution, the more difficult it becomes to effect the tail of the distribution by removing commodity pesticide combinations from the calculations. While removal most exposure

contributors results in a demonstrated change in the lower portion of the distribution, the exposures at the upper end of the tail, for example, the 99.9th percentile, are relatively unaffected by removal of a single commodity even if it is identified by DEEM as a frequent contributor to the high end of the exposure distribution.

And so we would like the Panel to please discuss the significance of this observation and its potential impact on the interpretation of the output distributions and the results from highly complex distributional analyses such as the Preliminary OP Cumulative Risk Assessment.

DR. KENDALL: Okay. At this point, Dr. Heeringa, would you lead off please?

DR. HEERINGA: I'll take a first crack at this one and my colleagues can join. First of all, I want to say that simulation tests of the types reported in addendum Table 1 and also shown in summary form in the presentation this morning, they're very important to confirm that the model is performing as we expect. And I think that as we get down to the development of these models and comparison, that these types of simulations play a very, very important role in the work that we're doing.

The simulation tests that produce illogical or unstable results or

seemingly illogical results. I believe that DEEM-Calendex should provide the ability to tag and replay the inputs for these simulations. So, in fact, you do have data, as I understanding Calendex, to go back and analyze the contributors to these upper percentiles.

So in some ways, I think there's a general problem here of distributional theory and a more specific problem of what happened in your particular simulation; and, hopefully, we can make those two consistent with one another.

Just a little bit on the distributional piece here. I don't want to bore individuals. But in a sense when we create these composite residues in a daily diet, we're compounding multiple distributions. And this yields a very complex composite distribution for daily residues intake. And this is a function of a number of factors. I'll just list those here because they may be explanatory in what's happening to you in this particular simulation.

We have to factor in the child's weight in kilograms, and this could be highly variable for children ages one through two because you're actually sampling people, children from the infants from the CSFII, and taking their weight in kilograms. So that divisor itself could have a factor of twofold.

And I'm not sure, given how diets are reported for these

children, I mean you put an apple on a high chair tray and about half of it goes to the wall and half of it goes someplace else and a quarter of it may go down the stomach. So those issues I think are there. I don't think that's going to be the answer, though.

The diet for the day, obviously, is very important in determining these distributions of total residue intakes. First of all, does the food appear in the diet? And there are any number of foods that could be considered. It's a narrower set for one to two year olds.

Secondly, if the food appears, is there a positive residue amount assigned to that food in the stochastic draw. If I recall correctly from previous reviews of these DEEM models and others, that in many of these foods, there's a high proportion that come from untreated or presumably zero or no detect residues. So even if the food appears, when we that the stochastic draw for the day of the residue amount, we may get a zero value for it. So there's a tremendous amount of variability.

And then for non-zero amounts, it's actually the value of the stochastic draw that does take place. If we think about the distribution, the means of the these distributions, essentially, because we're treating these foods independently, the means are essentially the sum of the individual expected values for all the contributing

distributions.

In other words, you have a distribution for every food component that could appear in that diet for the day. Obviously, the only ones that come into play in any significant way are the ones that are consumed during the day.

The mean of that composite for the day is going to be the sum of the means for the individual components that ago into it. Likewise, since we assume independence in our draws of these residue amounts for the foods, the variance of that composite distribution is also going to be the sum of the variances of the individual, non-zero food contributions from each source.

Removing food groups A, B, and C, as you've done in the simulation, changes the mean and the variance of this composite distribution. And, in fact, as I looked at this, my first response to your question is I don't see the problem here because it looked to me that the results from your simulation appear to be very consistent with what we expect, not just the removal of groups A, B, and C, A but even the sequential removal of A and then B and then C appear to produce a logical shift in the distribution of this residue distribution.

So the changes that you observed, and you actually acknowledge in terms of the form of the distribution rate, are exactly

what we would expect. So I didn't see anything unusual there.

The importance of foods groups A, B, and C to the composite distribution is quite obvious. You get a three-and-a-half fold decrease of mean MOE; a fourfold decrease in the 95th percentile. So, clearly, removing these groups is dragging the body of the distribution back toward the origin here.

Now, a 2.5 decrease in the 95th percentile, which I think is significant in many ways. And even a two-fold decrease in the 99.5th. But focusing on this 99 and 99.5th, which is your problem, the distribution of these quantities in this composite distribution is really somewhat unrelated to the distribution of the composite itself.

In other words, we can do a lot of things to the body of the distribution without being able to influence this extreme tail and really a function of the extreme values generated under of -- and not so much the function of the mean and particular variance of the composite distribution.

If you think about it, if I were to analyze the DEEM inputs to the particular simulation, if you think about how foods A, B, and C can contribute to extreme values, there's really two ways. One of them, is A, B, and C can form a stepladder. They are big. They are prevalent in the diet. They may have large residues. So they serve as

a stepladder.

And then we come along and we get another extreme value on a less commonly consumed food and added to that A, B, C value, it puts us into the extremes. So essentially, A, B, and C are boosting some other not so extreme values from other into the extreme.

The other way you can get it is that A, B, and C could actually be generating the extreme values themselves. And i think the basis of your question, you're sort of assuming, well, I removed A, B, and C, so A, B, and Cs extreme values aren't there. So why aren't the extreme values changing in the distribution.

Well, the only thing that you really removed is you removed the ability for A, B, and C to boost something else up or for A, B, and C to generate its own. Now the probability that A, B, and C in a mixture of diets is going to generate those extreme values all on their own is relatively small because there are only three groups. And if you think about it, even if the entire residue distribution were based on A to get to the 99.5th percentile, you essentially have to something with odds of almost 99.9th percentile, you have to have something that has odds of one in a thousand of being drawn from a distribution.

So the probability of getting an extreme event from A, B, and Cs residue distributions extremely small; and even in combination, it's

pretty small. So what happens here is that you've got 69 other food groups which might occur someplace in some child's diet during your simulation run and each of those 69 food groups also has extremes, and so as I sum across all of these children in the particular profile for a given day, someone is going to eat these odd foods.

And although they aren't as prevalent in the diets as A, B, and C, the sheer numbers of them that could be there and the fact that they could each contribute with some low probability an extreme value, essentially the strength in numbers means that you're still generating extreme values from all of these low prevalence food groups; and so these maximums are not being affected as much as you might think.

That's my statistical explanation. In other words, you have several different routes. And that what's happening is because you are still generating potentially with low probabilities but add small probabilities across large numbers of food groups, you generate higher probabilities for generating extreme values from these sort of nonprevelant foods.

I suspect that that's what's happening. This is a guess. And you'll be able to affirm that with DEEM. We can't rule out what I think are more pathological explanations in a statistical sense. That there may be some -- and this is what I think you're hunting for --

extreme residue commodity potency factor relationships in DEEM that don't make sense and are producing these outliers. Clearly, you want to hunt those down and try to rectify the data there to make sure that it is consistent with empirical data that you have on these distributions.

Also, another factor that occurred to me is that potentially, even though -- and this is really a stretch but I think it's worth looking at in your analysis. If you remove food groups A, B, and C, we're only looking in the simulation at a short one year interval. But most of us know that children's diets change considerably over that one year interval.

So it could well be that what you're doing when you remove A, B, and C is that you're actually removing foods that are eaten later in the interval, like whole fruits and vegetables, as opposed to sort of mushed fruits and vegetables or other types of cereals at the beginning. There may be some time-related dependency between food groups A, B, and C in the year one to year two.

And why would that be important? It would be important because the it affects the weights of the these children. The weights of these children could be actually the kilogram divisor in the exposure could be changed.

So those are, again, the last is a bit of a stretch. But I think if I had to analyze how to decompose the problem, theoretically, I think what's happening is that, as you draw out A, B, and C, you are in fact contracting this distribution significantly, pulling the body of the distribution back toward the origin, but you're not able to impact the very extremes because you still have this underlying, very thin extreme value distribution for all these other components.

DR. KENDALL: Thank you, Dr. Heeringa. As you can hear, there is music next door. We did not know this. We were only informed this morning that apparently there is to be a concert in ten minutes. So I'm going to -- which started even earlier. And, quite frankly, apologize for this happening. We were just notified a couple of hours ago. So we're going to take our lunch break beginning at approximately 11:30.

I ask everyone to bear with us for the next ten minutes or so. I hope that will work. And they'll be concluded by 1230, and we'll reconvene. So let's grin and bear it. And, Dr. Reed, can you follow Dr. Heeringa, please.

DR. REED: Yes. I just want to commend the Agency for the enormous task and a lot of work put into it. It's impressive.

What Steve was saying, I totally agree. It's a very complex

analysis. I'm sure if there is an easy way to go back and see what happened to it or in terms of what is the major contributing factor except to do what you're doing. And that's something we do very often in our program, too.

I think even down to look at the CC to identify the high contributing commodities takes some looking around. You've looked at three of them. I want to follow what Steve was saying in that, actually, after you get rid of three of them or even one at a time, look at the CC again and see if you're right on track.

Also, when you look at the CC, as Steve pointed out, see that the H vector would come in to play within that 3-to-5, 1-to-2 bracket. The eating pattern, the distribution of contribution from different commodities, that sort of thing. A lot of times we have to go back and forth and find that high contributing commodities that way.

I'm sure there are many more sets of sensitivity analysis that could be done. Something was mentioned -- and I thought it was worth sort of mentioning again -- was the curiosity of whether chemicals will make a difference. You're looking at commodity; contribution, look at the chemical contribution.

Other things are -- I mean, in that case, you sort of trap the high contributing chemical and then do as you did, removing one at a time

and to see what happened.

In terms of things to consider, I think there's so many things to consider. But the Agency is under the time constraint to complete something at this time. What I was thinking was as the most important thing is this: From the presentation and the document, it reflects a lot of experience from the Agency in doing what you do and giving the assumption that we assume, for example, dietary exposure does not fluctuate significantly over the year, that type of thing, or even though it's calendar-based in terms of the whole assessment but dietary is not. You know, these assumptions, PDP data, single unit analysis data, will not impact a whole lot as compared to using composite.

I think the Agency has lots of experience with this. It would be good to present it in a way. I think people would like maybe to see some support instead of just a single sentence statement. I think that would help.

DR. KENDALL: Thank you, Dr. Reed. Dr. Zeise, would you like to follow, please.

DR. ZEISE: I agree with the comments earlier, and I think the explanation provided for the finding is very reasonable. And, obviously, we need to explore to see really what is happening in the tail and whether or not there is a problem with the model or whether

or not that explanation that was given holds up.

In addition to exploring that, I think it's very important to focus on the tails. It represents many individuals in the population. And it's important, I think, to explore other factors that might change the tail significantly. It's not clear the extent to which violated exposure would change that. The extent to which consideration of degradates might change the assessment.

And then the issue -- and I didn't see it explored in the document -- of binge eating and seasonality of fruits coming in in the summer months, and so forth, if CSFII appropriately captured some of the cases where you might expect larger exposure. I think that would be useful to explore.

And the nondetect, I'm assuming that that has been adequately addressed. There was a discussion in the document. It wasn't clear to me the extent to which, if you assumed at the high end of the distribution, if you threw in some nondetects as half the detection level, whether or not it would significantly change the evaluation at the tail.

And the reason why it is so important to look at the tail is that the MOE is rather small there. In fact, if there are even larger exposures than that, that really indicates that there is a problem. So

really understanding that region is important. And I'll leave it at that.

DR. KENDALL: Thank you very much. Any comments from the Panel in addition to the comments already made on this particular question?

DR. MCCONNELL: Yes. I was struck by the fact that you depend a great deal on the UDSA for a lot of your input in your calculations. I was wondering, and it was suggested by one of the people from the audience, that you have relationships with UDSA. I don't know what they are. Do you have periodic meetings with them to update yourself with what they're doing? Their science must be evolving as is your science, and do you have a way to keep up with that?

DR. SMITH: Yes, we do. In one area, of course, one of the major areas we're discussing today, are the residue data that we're using. That's the PDP program. And we work very closely with them. We advise them as to what our interests are and then things we'd like to see done from year to year. So it's a very close relationship. Also, there has been considerable interaction in the area of the CSFII. I don't know that I can say much more about that; other that I don't know if, David, is there anything you'd like to add to that?

MR. MILLER: Yeah, we do communicate with USDA on the

CSFII and the food research group that is responsible for it.

DR. DURKIN: Thank you.

DR. KENDALL: Any further comments? Dr. Durkin.

DR. DURKIN: Very briefly, we will be discussing residential exposure at a later time. But this does relate to food and, again, it is the issue of homegrown vegetation. I did not see that in the residential exposure. And we may clarify it then. But it's clearly not in your food exposure. And I'm rather concerned that that could be the 800-pound gorilla.

The concern is with people in a rural area, especially rural south, who may live in a region of agricultural usage that could be very high. And I am a little concerned about what I've heard up to this point that we could have, again, a bimodal distribution of risk that we're simply not addressing.

DR. KENDALL: Okay. Any further comments? Mr. Lewis, our DFO, has informed me that they're running late over there. Therefore, we may have time to go to the next question. I'd like to take an hour break. So could we procedure into the next question as recommended by the best intelligence information I've got. And it's the military next door.

MR. MILLER: The Calendex model can be used in a number of

modes to develop a profile of exposure estimates. In the current assessment, OPP conducted a series of single-day assessments arrayed chronologically to develop a response surface of exposures. A constant percentile of exposure was selected to represent the potential exposure to a given percentile of the population. For example, the 99th percentile for each day would be arrayed for 365 days to reflect the population estimate across the calendar year.

Calendex can also be used in a multi-day sequential series analysis, asl referred to as a "rolling time frame mode." A rolling time frame provides an estimate of the average of daily exposures for an individual calculated over multiple (7, 14, 21, or 28) days for each multiple day period over the course of a year, (e.g., days 1-7, then days 2-8, then days 3-8, etc.).

In this model, an individual's food exposure is tracked across the calendar year by randomly selecting day one or day tow of that individual's reported consumption from the CSFII and combining each commodity which comprises that consumption with randomly selected residue values for each day of the calendar year. These rolling averages for each individual are assembled to develop a distribution of rolling average exposures.

During previous SAP meetings, the Panel has expressed concern

about the use of CSFII records to represent longitudinal consumption patterns for individuals. Concern arose as a result of the design of the CSFII study, in which two nonconsecutive days of data (separated by 3 to 10 days) were collected for each individual.

Please comment on the use of CSFII data to support each of these two modes of Calendex as they pertain to the cumulative risk assessment of pesticides in foods.

DR. KENDALL: Dr. MacDonald, can you lead off, please.

DR. MACDONALD: Well, I guess to begin with, I'm under the impression that CSFII is about all we have that's relevant. So we don't have a lot of choice here. I guess there would scope for doing some kind of sensitivity analysis to see what the impact would be of having, say, you could make up some data on longer term records and just see what impact it would have on the estimates.

As far as the different modes of running the Calendex model goes, I think Dr. Portier's remarks earlier were very relevant. And I hope they'll get into the response for this question.

But, basically, I think the effect of using the rolling average is it will mitigate effects of sampling nonconsecutive days to some extent; but, mostly, it will just reduce the extremes in the simulation.

Is this relevant? I don't really know. I think we have to know

more about the metabolism of the OPs in humans at different life stages. I think the limitation here is the margin of exposure computed as the point of departure divided by exposure, so we have to make sure that the exposure measure and the point of departure are both relevant.

For example, what we saw yesterday in the adult rats, the dose response curve, we saw there was a shoulder and in many cases in that suggest in some situations a moderate short-term exposure is totally innocuous. But that's for adult rats. As the NRDC has pointed out, it might be totally different in humans; it might be totally different in human infants and fetuses. So it's really hard to say what the effect of changing your exposure measure is going to be if we don't really know what type of exposure is most relevant in the population we're considering.

I think to conclude, the rolling average is probably a good idea if the main concern is chronic low to moderate levels of exposure. But if the real concern is acute levels, than reducing the extremes is perhaps going to be missing some of the more dangerous episodes.

DR. KENDALL: Thank you, Dr. MacDonald. Dr. Freeman.

DR. FREEMAN: The two methods used with Calendex, you can almost think of them as bounding examples. The use of a single-day

constant percentile of exposure for every day provides an exceedingly conservative estimate of exposure. It is clearly not representative of individual exposures over time. And I find it difficult to understand what it actually means in terms of population exposures. And, also, I'm not quite sure how you're going to use that.

In contrast, the second method which uses the rolling averages, is not only less conservative, but for very young children when you only have two samples of food, may actually reflect what young children over a limited time period, as Dr. Heeringa was suggesting, is fairly realistic. Young children tend to have very narrow food habits. So that while you only have two samples to draw from, they probably aren't that different from each other because the children aren't eating a wide range of foods. So that may actually be useful in representing sort of the average young child with fairly limited ranges of foods in their diets.

On the other hand, that same rolling average, because you only have two food samples to work with, may underestimate or suppress the high-end exposures from diets in the same children. And I'm not sure what you can do about that.

A concern of mine is in the application of all this stuff. In the examples that you give, you suggest that diet is treated as uniform

throughout the country. And unless you have already done so, I think this is a hypothesis that needs to be tested, particularly in areas such as Region 3, the Texas Fruitful Rim, which are predominately Hispanic. I wonder whether the diet for based on the CSFII for the total United States is really appropriate. And one thing that you could do is to compare the diets associated with that region from one such as the Easter Upperlands or the Northern Great Plains where the demographics are very different.

Another alternative -- that also assumes that the CSFII has not under represented minorities in their sampling, which may also be the case. And if that's the case, you may have to go back and look at census data for those areas and do some sort of proportional weighting based on census characteristics.

So that adds more complexity to your model.

DR. KENDALL: Thank you very much. Dr. Reed.

DR. REED: I want to follow up on what Natalie was saying. I think, basically, if we take a sort of a common sense way of thinking, we would think that the diet has seasonality and has regional differences. Again, I think it's partly I think because of the Agency's experience in this area, knowing the impact of parting them out into region and season, and maybe it doesn't come out to be a whole lot in

terms of impact. And it's time consuming and it's not readily available in terms of tools right now with DEEM and Calendex. I'm not sure about that part.

But what I'm trying to say is that I think it would be good to give some support to that assumption or, as Natalie was saying, run some data sets. Remember, we've in the past looked into things that are important to children. For example, apples, they do have seasonality and also regional differences. It could be up to about 20-percent differences. So it's something that probably is worth looking into.

In terms of using that data for modical day sequential analysis, you have already presented the pros and cons. But I remember -- I just have one simple comment. I remember in September 2000, when we look at Calendex, there was the recommendation to look into this method. And I'm still very interested in following up on that.

That is instead -- I think maybe the overriding desirable idea right now for you is to trace an individual. And, therefore, you think that perhaps you need to stick with these two data points. But I think there's somewhere in the document that emphasizes that you're not actually tracing individual exposure pattern. So in that case, it is still possible, as what we recommended before, to base on demographic

characteristics, to pull the data together so that you would have a larger sampling size of population to draw from instead of just two points.

And I don't know how difficult that is. But I think that's something that's still worth looking into. I don't know if I'm clear on that point.

DR. KENDALL: Is that clear?

MR. MILLER: Yeah. I think what you're saying is when you say "pool the data," the way it's done now is each individual's diet is connected to that individual.

DR. REED: Right.

MR. MILLER: Each of those two days worth of diet.

DR. REED: Right.

MR. MILLER. What you're saying is maybe draw from, essentially a pool that has demographic similarity to that individual.

DR. REED: Right. Three to five pool with different seasons, four seasons.

MR. MILLER: Okay.

DR. KENDALL: Very well. Dr. Heeringa, anything to add?

DR. HEERINGA: Just briefly to Dr. Reed's comments. I think the idea -- right now, the way that you're using the CSFII data, is

essentially you're locking a child's body weight and gender and age into a particular diet or maybe at most three diets if in the CSFII and two diets for the infant and child observations in the '98 CSF.

And what we're doing there -- I don't think of us believe that this child is going to eat macaroni and cheese 365 days a year. But in your sample someplace else, there's a child eating green beans and a hamburger or there's a child eating oatmeal. So what you do is even though you're focused on an individual child, what you're assuming is exchangability among children of the same age and same gender. And the thing you're doing is you're locking a particular body weight to a particular diet.

I think that's a constraint you don't need to use. Dr. Reed's suggestion is essentially sample the child. You need to get a representative samples of children with their body weights and their genders and their ages. But then, among children in your national sample, which you're assuming to be exchangeable anyway, sample their diets to link to those on a daily basis.

So I think that breaks one sort of false correlation in your current input structure that is unnecessary and doesn't contradict in any way.

Now, on the other response to this question, you are

constrained by the fact that you have two or at most three days of diet for any individual. By putting things in this pool, you've sort of unconstrained people's diets a little bit. But you haven't actually built in realistic patterns. You still have to assume, if you go Dr. Reed's route, that you have random eating and that there are no consistent correlations over time in consumption patterns. Which we know for a bag of oranges or a bag of apples or a bunch of bananas or even things like green beans, you might be eating them two or three times during the week in which they're bought. I think that's another level of sophistication that you might think about bring in at least in terms of simulation.

And this is what Dr. Portier brought out, yesterday or earlier this morning, that you might look at some testing in the model where you do two things. And that is you have a lag factor in the consumption in the dietary intake for some of these commodities that we know are going to be in the household for a protracted period of time. And I don't think macaroni and cheese is going to be one of them. But apples and various fruits that are bought in larger quantities than vegetables, and see what that does.

And if you do that, then I think you, in addition to sort of introducing a lag in people's dietary consumption during the period of

a three- or four-day average, also preserve the draws on the residue amounts because it's only realistic if you do that that these commodities that came from the same source would be expected to have nearly similarly residues amounts. We know there will be variability, but much less variability than a completely random draw.

So I think with the data that you have available and some assumptions -- and, again, I would only put this in simulation context right now, to look at what happens when you introduce not only lagged consumption from one day or time-correlated consumption of some of these commodities for short periods. And I would say three to four days would be fine on most of these or a week. And then, also, to preserve the residue amounts associated with those.

Now, that's complex, I know. But I think that would add a little bit more reality. Now if you do that, then I think this whole issue of whether you use these rolling averages or individual days, the rolling averages make sense as a measure of sort of short-term chronic or maybe steady state impacts of the residue consumptions; but I think they only make sense if you do these other steps. And that is allow foods to have time correlation over short periods of time and that the residue amounts on those fruits are also preserved as draws from your residue distribution. Then I think these rolling averages do approach a

better reflection of what the sort of chronic exposure over a 28-day period is more likely to be.

I think if you're doing fixed diets for kids, random draws of residues everyday for each child. I'm not sure that you're getting from these rolling averages what you would really like. It's not a good reflection, I think, of chronic exposure. And the one-day stuff gives you the acute exposure in a better sense, I think.

DR. KENDALL: Any further comments from the Panel? Dr. Portier.

DR. PORTIER: I agree with all the comments that have come forward, starting with the one that said you guys did a great job on this. But presuming something we can look at and comment on is really pushing the edge of what's been done previously.

I was sitting here trying to think about my question earlier concerning the conservativeness of this particular method. Especially, the two-day flipping back and forth. And your observation that you think this is going to be somewhat conservative. And we had several questions about that from lots of the public yesterday, both the grower's side and the environmental side asked a question to what degree can we assume this is conservative.

So I'm sitting here trying to ask myself how do we assess that

without doing a full independent resampling scheme where everything is independent. As Ruby pointed out, you sort of have two extremes that you could do. The first extreme is the individual day data, run it for 21 days. But that's exactly the same as the distribution for the individual day. Taking the average of that over the 21 days is going to give you exactly the same distribution. So you've got that one. That's one extreme.

The other extreme is everything is random. Every day a new draw, a new diet. Everything is completely random. That's the other extreme in the sense that we know there are probably some correlations in there.

But we know something about the other extreme. If your distributions are normal, which they're not. Them I'm going to choose the simplest case here. If your distributions were normal, you know that by averaging over 21 days, independent normal random variables drawn on a day-by-day basis, the 99.9 percentile, in fact, any percentile except the 50th percentile, is going to change by a factor of 4.6; the square root of 221.

If it's log normal, you can actually calculate the same things. The 99.9th percentile. But it's not a constant. The 99.9th percentile change is about a factor of 12. The 95th percentile change is about a

factor of 6.

But the point there is you can look at your two-day consecutive draws, compare it to your extreme single-day case, and ask yourself, have I dropped the 99 percentile and the variances by some number that appears to be in this range or less. So is it on the conservative side or on the independent side?

Judging from your quick graphs there, David, it looks like it's on the independent side not on the conservative side in terms of a very consistent redraw. But I'm not sure because I don't see the full distribution for that.

But I think you could address it that way. You might see some mean shifts as well which could tell you something about theoretically how conservative that approach might or might not be.

But I agree with everyone that you need to try some other things, potentially theoretical or to resampling technique.

DR. KENDALL: Thank you. Any further comments from the Panel? Dr. Rhomberg.

DR. RHOMBERG: Just briefly. And I hope this is the right place to raise it. On the single-day analysis, you know, in the end what that is able to show is seasonality. Otherwise it's just doing the same thing over and over and over again and they're just replicates.

The only thing that's really different between one day in January and another day in May is seasonal differences.

And I guess I was struck by the fact that there didn't seem to be many, that if you looked at those graphs, including the one that's right on the front of the report there. Yes, there's some variation up and down; but there's no big sway, no big seasonal sway of going up and down.

And my question is why is that? I would really have expected at least some such effect. And the only reason that there wouldn't be any is if seasonal effects are at all important, that they are somehow excluded here. Would that mean that seasonal effects are driven maybe more by seasonal effects on food choices than they are by seasonal effects on residues or what? I guess I'd just like some discussion of why there isn't more seasonal effect there when one would expect some.

MR. MILLER: I'll say we're not -- when we use the PDP data, we're not taking into account -- and it's just clarify it. We're not considering the seasonal effects of when the food is sampled. So there is no seasonal component.

When I said we start with January 1, it's not necessarily a diet that a person reported eating on January 1. So for example, when the

CSFII went out, they didn't -- the January 1 diet is not specifically a January is 1 diet. It was essentially the seasonality component is added to the assessment by means of the drinking water which is seasonal. We take into account the season there and the residential uses.

DR. KENDALL: Any further comments? Yes, Dr. Zeise.

DR. ZEISE: I just want to reinforce the idea that when you consider the averaging period, you carefully look at the pharmacokinetics in humans and determine what makes sense to do. It might make sense to actually build in a pharmacokinetic parameter to address the issue of persistence across time.

DR. KENDALL: Very well. We understand now the program next door may go as late as 1, so I'd like to try to move into 2B. We are tracking their program. I think somebody is speaking at this time, to be followed by a concert. The concert is going to blow us out of this room. So let us push forward.

Today's one of those challenges. We will take a break for one hour. And I will see you for 1 o'clock. Thank you very much.

[Lunch recess.]

DR. KENDALL: We'll go ahead and get started. This will reconvening the SAP. The point at which we are currently is

addressing Question 2B. Please read that question, Mr. Miller; and we'll go on from there.

MR. MILLER: The random PDP residue values assumes that the residues in foods consumed across a series of days are independent of each other. In other words, foods consumed are from unrelated sources and there is no carryover from one day to another. This assumption may be inappropriate given that many consumers obtain food in bulk (i.e., multi-day) quantities that may have similar treatment history and would typically consume this food over a short multi-day period (e.g., leftovers). In such a case the residues contained in the foods would violate the assumption of independence.

Please comment on the use of PDP data to support each of these two modes of Calendex as they pertain to the cumulative risk assessment of pesticides in foods. What issues are likely to accrue from the assumption of independence in residue data?

DR. KENDALL: Dr. Reed, can you lead off, please.

DR. REED: In terms of single-day exposure mode, I don't have a lot of problem with it. As long as it was clearly stated, you know, what the announce is about. I think the only issue that we're been throwing about is the composite nature of the data.

We knew that from single-eating-size analysis that you would

have essentially higher, possibility to a higher, residue in a single-eating-size sample. But that's for a single chemical. And I don't have any feel about what is it going to look like for index equivalence-type of residue data base.

So I would really appreciate that, again, I think that assumption was that there's not a substantial difference in it. And I think it would be good to present something like that in the documents so a reader could understand and follow.

In terms of multiple day rolling average, I think PDP data is suitable for that, especially when the composite is not a problem. I'm not sure -- or I am sure that this does not really address the carryover, leftover, or same batch exposure scenario. I would go about and find the heightened contributing commodities and see if linking days would make a difference. I would not offhand go in and link everything from day-to-day yet.

The reason I say that is because I think linking days would be really specific to certain foods. You know in the past we talk about Thanksgiving meal and that kind of thing, also the buying-eating pattern; people buy a bag of apples and eat for how many days; shopping pattern and all of that.

That being so, I think what I'm thinking is it's important to find

places where it might make a substantial difference and not just shotgun and go in and do all of that. And I'm thinking of that mostly in terms of resources. And I'm thinking of now of approach and risk assessment is about. You decide when and why you want to go in and refine something so that you're more focused and you're not spending a lot of time and effort.

That goes back to the comment that I made earlier that it is important to make a clear presentation in terms of what are the assumptions and why you think so; and so when it comes to the steps whether we link days or not, it would be much clearer as a choice or not.

DR. KENDALL: Thank you. Dr. Heeringa.

DR. HEERINGA: I very much agree with what Ruby has just presented. Just a few added comments.

In response to the earlier question, I mentioned exploring the issue sort of continued consumption of a single food item over several consecutive days. Again as Ruby has just pointed out, it requires modeling, buying, and retention patterns within the household. My sense is that even has something sort of three to five days retention of a fruit or vegetable batch would be an appropriate bound to set on testing that.

Clearly there if you do that, then I think you want to preserve the sampled residue amount over those three to five days, also, to preserve that correlation which you would naturally assume in the purchased food product.

With regard to the independence on a single-day analysis, I think the independence assumptions, since you're doing it on a daily basis, it really doesn't come into play. It's more when you look at sort of chronic or accumulating over multiple day analyses that I think you need to take into account the correlation, not only in foods eaten, but also the residues on those particular foods over the days.

One additional comment to, I guess, related to the question, that is, the use of OPP residue data base. I believe that most of these are composite amounts. We're not only compositing the servings over the day, but we're also compositing the residues over multiple articles. If anything, I think that would tend to attenuate the extremes that we would observe on a daily analysis.

So if anything, it's probably a little bit anti-conservative to use the composited, samples as opposed to some strategy which I know we've investigated in the past to try to derive a single serving or a single-serving residue amounts for use in these analysis.

DR. KENDALL: Dr. MacDonald. Thank you, Dr. Heeringa.

DR. MACDONALD: I don't have a lot to add to Dr. Reed and Heeringa. But I will express my sympathy for what I see what must be a very frustrating situation because there are just limitless ways to start making these models more complicated and you'd really like to know ahead of time which of these ways are going to be worthwhile.

I guess all I could suggest here is if you -- I don't think you even have to do a pilot study. If you could make up some the data with the consecutive days or with the correlations built into it and just try some small simulations and see what kinds of differences it makes.

Certainly, that in the other context, the study you did with the A, B, C gave some -- it seemed to be a very simple thing to do, but it gave a very useful results fr what would happen if you change some of the data. And maybe you could devise something like that with the correlations.

DR. KENDALL: Dr. Zeise.

DR. ZEISE: I don't have a lot of add to the comments that already been made. We've talked about this this morning as well.

The one thing I would add is that there are likely to be differences across the different age groups in terms of the extent to into which this comes into play. And particularly for the younger age groups, one would expect a lot more similar behavior from day to day.

As an upper bound kind of analysis, one might assume that every day they consume the same value or sample between the two days.

Another possibility comes to mind along the lines of -- I like the idea of the correlation analyses that have been proposed. And another possibility would also be to do some scenario plane to kind of test and speculate what could be happening at the extreme by looking at different scenarios for some high consumption of foods, say, during -- I don't know -- watermelon season or when you might expect very large consumption of fruits more so than other part of the year among certain subgroups.

DR. KENDALL: Good point. Any further comments from the Panel on this issue in food exposure? Dr. Portier.

DR. PORTIER: Not specifically on this. Well, let me ask a question on this one first.

Steve was just asking me, and I guess we're both a little confused about the issue. If the PDP data set has a residue that exceeds the limit, you still include that in the analysis? Yes or no, you take those out?

DR. SMITH: We take out residues that exceed tolerances, yes.

DR. PORTIER: Then I think from my perspective, I would recommend you not do that. I think it's going to be there's two

reasons. One is it's going to happen no matter what the tolerances are set; there will be samples that exceed the tolerance. That's the first.

The discussion we had of where PDP data comes from and the question of what happens when people buy things in the market or from not necessarily the large commercial sources, there may or may not be higher residue levels depending upon when and where, et cetera, where they buy it. And those things are just unknown. My recommendation would be that you include them in your over all analysis. And I don't know how the rest of the Panel feels about that.

The other point I wanted to make, which is more general, is yesterday we had a discussion about point of departure for margin of exposure from the point of view of hazard. And much of our discussion pertains yesterday pertains, also, here especially to some of the public comments which had to deal with the quality of an estimate of the 99.9th percentile.

I think one could argue that choosing a distributional point from which to compare margin of exposure could be driven by the science, find some optimal rule for deciding what seems supportable by the science that you're working with, and the margin of exposure process is adjusted based upon where that percentile is and the quality of the science that went into that exposure percentile.

I think that would potentially be a better solution than the continued debate about the quality of the 99.9th percentile. And I think I'll add that to my comments to you.

DR. KENDALL: Would EPA like to respond to that? Dr. Roberts.

DR. ROBERTS: Yeah, Chris asked how the rest of the Panel feels about the issue of including the violative residues from the PDP in the assessment. And I guess I would weigh in in favor of including them.

I think that as a follow up to some of our earlier conversation, I think that this probably is an unavoidable consequence even of the lawful use of pesticides despite everyone's best efforts. It's a human exercise, and there's going to be a small percentages of times when those levels are exceeded. And I think if we're going to make the argument that our cumulative risk assessment reflects reality, I think it's probably important to go ahead and include those small percentages in our assessment.

DR. KENDALL: Any further comment or agreement? Dr. Durkin.

DR. DURKIN: Yeah, I would like to simply endorse the idea of putting the residues in. I understand why they're not there in terms of

not being able to address them perhaps from a regulatory perspective and that does make a great deal of sense.

But we seem to have two tracks here, and we discussed this. Are we dealing with a regulatory tool, or are we dealing with some sort of a public health risk assessment? Do we have a problem here? And if that second part is important, and I believe it is from what I've heard, then I don't see a reason to exclude those residues. In fact, I see every reason to keep them in whether or not they make a great deal of difference. We're trying to reflect reality.

DR. KENDALL: Dr. Bull.

DR. BULL: He said it much better than I, but I agree with that.

DR. KENDALL: Okay. Dr. Rhomberg.

DR. RHOMBERG: I guess I'd like to take an agnostic position on this, but with a little discussion.

It seems to me that the purpose of doing the risk assessment is to serve risk management ends. So the real question is what risk management options that are available and what kinds of analysis would most inform them?

Now, you could imagine violative exposures, that being an argument for including or for excluding violative exposures. And in a way it sort of depends on some things about how inherent they are in

any kind of use of the agent as Dr. Portier was suggesting. Obviously, to some degree that's true.

But if you put them in, you have to be very sure that you then interpret the analysis accordingly. And if it happens that those violations are driving the upper percentiles, it has to, then, be acceptable to do a risk management solution that sort of takes that into account and takes into account what perceived responsibility there are for different parties to deal with the fact that that kind of things occurs.

So if we put it in, we have to be very clear that the analysis means sort of something different from a risk management point of view. We can't play it this way one time; and then when the Agency is going and making the risk management decisions, playing it the other way and to try to say, Oh, it's incumbent on the Agency to make regulations such that those things don't occur as well.

Whether they are not, is a complicated question that isn't really about exposure analysis anymore. I think that if we put them in, the analysis means something else; and it should be clear that we are expecting a different use and interpretation of it by the EPA in the regulatory arena as a result of that.

DR. KENDALL: Dr. Adgate.

DR. ADGATE: I mean not to beat the dead horse too hard. I think it would be useful to point out the fact that tolerances are in fact not health-based and that should provide you with some cover. And I think that fact you are all quite aware of often gets lost in these sorts of analyses. At least in theory what we're doing here is health-based.

DR. KENDALL: Dr. Portier.

DR. PORTIER: Following up on what Lorenz said, I guess the only regulatory control that would convince me you should throw out the violators would be one in which you were continually monitoring these products, and if it exceeded the tolerance, you threw away the product. If you didn't throw away the product but in fact mixed it with product with lower bounds, lower levels, then that could, of course, be incorporated into the sampling strategy for the PDP to look at the question of what impact could would that have. But I think the reality is those are the data and I would really encourage you to use them.

DR. KENDALL: Would EPA care to respond to any of the points made, or were they clear enough?

MS. MULKEY: I think we would like to encourage a little more elaboration if there is going to be a discussion of some sort -- and I'm over simplifying this -- trade off between choices about what part of

the distribution to consider regulating at and what kind of acceptable or target MOEs we might work with. And we are mindful that that is that's a mixed science and policy decision as you seem to be mindful. But if you're going to discuss the idea of the intersection between those two, do so in more that identifying it as an intersection, I guess is what we're trying to say.

DR. KENDALL: Okay. Anybody like to comment on that? Chris, do you want to comment? Lorenz? Go ahead and start, Chris.

DR. PORTIER: You know we've discussed this from the other direction before with the SAP in terms of using the benchmark dose and what happens with 1 percent, 5 percent, et cetera. On the side of exposure, I think it's got to be the same thing. And I don't have any fixed factors for you. I think it's a debate you have to have both publicly and internally as to how you do the margin of exposure and what constitutes a reasonably acceptable margin of exposure.

It's driven by a lot of things. In this case, instead of looking at a directly toxic endpoint, you're looking at potentially a biomarker of a toxic endpoint. And that weighs into your decision about how big or small you want the margin of exposure.

I think the same thing is true on the exposure side of that distance. In terms of, if you only have 10 or 20 or 13 samples from

which you're making your distributional assumption, you would want a larger margin of exposure against a fixed point. And that pertains -- it pertains to the variance of the estimate of the point.

If I choose a 99.9th percentile, I know the variance is going to be large; and I know, to some degree, that my choice of that percentile is driven a lot by tail behavior of my data set. So the bigger the data set, the less of a margin of exposure I would want if I believe 99.9 percent is really safe.

If I believe 99.9 percent is safe and I'm going to set it at 90 because that's the best thing I can do with the data set that I have, then I'm going to want some sort of factor in my head for this margin of exposure that makes it a bigger margin of exposure. Because I know chances are 10 percent of the population is somewhere above is, but I'm not sure what, how far above that actually goes.

There are no easy answers in that question. But I think we have to be as a Science Advisory Panel, we have to be clear where the science can take you and where it can't. And by deciding on a margin, deciding on a point of departure that's based science per se with reasonable objective rules and recognizing that sometimes the science pushes us closer to the tail of that exposure distribution and sometimes it doesn't, I think that needs to be factored into the margin

of exposure rather than always choosing a fixed point, 99.9, regardless of the quality of the information and a fixed margin of exposure against that.

DR. KENDALL: Okay. That's pretty clear. Dr. Durkin.

DR. DURKIN: I was going to weigh in with something a lot more simplistic. I think basically philosophically agreeing with what Chris has said here.

We are talking about margins of exposure and talking about these as things that can be basically set as a matter of policy. But I think it's good to keep in mind that for a very, very long time, the EPA and others involved in human health risk assessment have sort of looked at the reciprocal, the hazard index of chemicals, that was in turn based on a ratio of the exposure to the RFD, where the RFD was something that was pounded out as a matter of science to the extent possible.

And I think that this is -- you can still handle it as a margin of exposure if you're comfortable with that; although I think the hazard index approach is much more elegant. That's just my bias.

But I think the point is that we know a great deal about the organophosphates. You have picked yourself an index chemical, and we have, I think all, agreed that this is a reasonable approach and that

the relative potency method is reasonable. I don't think it is beyond the scope of OPP to look at whatever choices that they would like to make in terms of do we regulate at the, you know, 99.9 or the 99 or whatever, and then to look at both animal and the human data that we have, not simply methamidophos, but on the whole class of chemicals, and come up with what is functionally an RFD or, if you're old an ADI. That would indeed lead you directly to a margin of exposure that is more science-based than policy based. And I think that would probably be a reasonable way to go about this.

DR. KENDALL: Dr. Reed.

DR. REED: Maybe this is a good time for me to get something clear. I really appreciate in this, whether it's uncertainty or a sensitivity analysis or the material that we received, that you actually present not just one slice of the distribution, 99.9th or whatever, but that you actually present modical points.

I don't know. Are you thinking of doing that in the final document, or are you thinking of just presenting it one point?

MS. MULKEY: In almost all our risk assessments, we present these multiple points.

DR. REED: That's my understanding. Because to me, that's important. I think a lot of problems or lack of understanding about

when you read a document is that it's really bothersome if somebody just presents one point to me. It depends on how you slice it. The high end gets sliced off or high end gets included and that kind of problem.

Thank you for that clarification. I would like to see multiple points being presented.

DR. KENDALL: Dr. MacDonald. Okay. Dr. Bull.

DR. BULL: Just a quick point. I think it's building on what Chris started off here with. But one of the reasons I asked my question related to this earlier was I think you pick your point on the distribution, you may find that regulating at the 90th percentile will have absolutely -- taking your margin of exposure at 90th percentile, no matter what it is, the way I see the data there is some possibility you'll never affect the upper end of that distribution because those are going to get every more rare events as you get out. And when we come to the drinking water thing, that's what concerns me. If there's a hazard in drinking water, it's a very extremely rare event. And might be an important event.

But you're probably not going to change that by either adjusting, you know, within some reason between the 90th and 50th percentile on the way you deal with residues on these different fruit

crops. It's probably not going to effect those extreme values.

DR. KENDALL: Okay. This will conclude our food exposure assessment, unless there are any further questions from EPA for the Panel.

Okay. At this point I'd like to move us to drinking water exposure. And, Dr. Perfetti, would you like to introduce your scientist.

DR. PERFETTI: To do the water presentation, we have Nelson Thurman and Kevin Costello.

DR. KENDALL: Welcome.

MR. COSTELLO: Thank you give everybody a chance to get a hand out.

Good afternoon. I'm Kevin Costello and today with Nelson Thurman here we'll present a summary of the work we did designing and performing the drinking water exposure assessment OP cumulative risk assessment.

First, a road map of today's presentation. First of all describe the preliminary results of our assessment so that everybody can consider the rest of the presentation in that context. I'll describe the background which led up to our assessment, first reminding you of the data requirements we had for the exposure assessment. And then I'll

describe the knowledge we already had about the organophosphates in drinking water, what data we had available, and just briefly review the guidance we had received from the SAP in the past on the building blocks we used for this assessment.

Finally, Nelson and I will discuss the drinking water assessment as it appears in the December 2001 Draft. As we do, keg in mind the two questions that we posed which deal with the two issues basically presented here. First, the watershed modeling approach that we took for the drinking water exposure assessment; and, second, the regional assessment approach that we took which differs from the nationwide assessments we've done for individual chemicals.

We'll try to do our presentation in a way that clarifies, builds on those questions so that everybody understands better what it is we're looking for.

Although Nelson and I are the ones giving the presentation today, we're actually part of a much larger team that worked on this basically from March until the December legal deadline and completed it in time.

You can see that on the team from EFED beside us that we had ad hoc teams that worked to come up with new modeling scenarios. And Ian Kennedy worked to get the model development together. We

have some folks working on a separate track for an SAP on water treatment effects. There are people from other divisions such as HED and BEAD helped us with all the usage data and with building regional assessments.

Now, the preliminary results of our exposure assessment indicate that drinking water is not a major contributor to the total cumulative risk from organophosphate insecticides. In fact, the assessment showed that the exposure from drinking water was up to an order of magnitude or more below of the food exposure.

Because of this result, it's very important to us that the Panel think in terms of whether, as we give the presentation and from what you've read, are there any systematic flaws in our approach that would lead to over estimations or underestimations of possible drinking water exposure. This is really important not only for the OPs, but this is the tool, this is the first shot at the tool, that we intend to use for future cumulative risk assessments for other pesticides families.

DR. BELL: Can I ask a question? I can't read this either there or there. And I'm trying to figure where we're at. Is this dealing with some level of residue?

MR. THURMAN: Actually, I think the whole part of that was just to illustrate. Basically, when you get above the 95th percentile,

you see the similar trend.

DR. BULL: So it's above the 95th percentile.

MR. THURMAN: It's a higher percentile. And the whole intent of it was just to illustrate that.

MR. COSTELLO: So as Dave Miller presented before, and as SAP has seen before in the case study, the cumulative risk assessment was done using a calendar-based approach. And daily exposures in water are one of the building blocks of this approach.

Now, for the OP assessment we used the daily time step as described before. But in future assessments, it could be -- that an error there. Calendex will allow the 7-, 14-, 21- or 28-day rolling averages we've gone through. And, also, as described earlier, Calendex is the tool used to combine these exposures from the different routes.

This is important especially for the drinking water and the residential exposures because they have seasonal differences, they have pulses of exposure that we consider in the assessment as opposed to the food.

So we knew that in order to work with Calendex our water assessment had to provide a distribution of daily concentrations for the probabilistic exposure assessment. We had to account for

variations in time, daily, seasonally, yearly. We had to account for variations in place because drinking water is much more of a local phenomenon than food because of how food can be distributed the around the country. And we needed to reflect the possibility of co-occurrence of multiple OPs for cumulative assessment as they occur together in place and time.

When we started this, we were not starting from scratch. We already had, from the previous five years, more than 24 individual OP assessments in the interim routes that had been done. From those, we were able to derive the pesticides properties, the physical chemical properties of the chemicals that we used to figure out environmental fate.

And on top of that, because of those, we had regulatory actions that had been taken voluntary cancellations, use rate changes for many of these pesticides. And as was described before, as uses were taken out, they were no longer considered in the assessment.

On top of that, we had a great volume of monitoring from surface water and ground water; and to a lesser extent -- I'm sorry. Can you go back one.

And we had the individual drinking water assessments that were done in the aggregate human health risk assessments done for each of

these routes.

And finally, very importantly, we had SAP guidance along the way as we refined our process for doing drinking water assessments.

Now, as we look through the available monitoring which had in fact grown in volume since we did the individual assessments, we found that in fact the OPs are found in drinking water sources. Although this is not frequent, and they're usually not at high levels. When considering all kinds of water monitoring, not just drinking water, surface water sources, generally, seemed to be more vulnerable to contamination by the OPs in a pattern that was seen not only in nationwide programs like the NAQUA Program, but also in the state programs because we actually contact all 50 states to see what kind of monitoring they've done over the last 10 years or so.

Chlorpyrifos, diazinon, malathion were the most frequently included; but they were also the most frequently found in surface water studies, ground water studies and drinking water studies. We found especially from the NAQUA Program that co-occurrence of the OPs in water is likely. Multiple OPs were detected together in individual samples. And this is not surprisingly related to usage in a particular watershed.

In looking another the monitoring, however, we did find that

there some limitations to what was available for our purposes. Most importantly, there is no single definitive study that can answer the question what OP exposure is in drinking water. So we knew we would need to look in monitoring in a weight-of-evidence approach from several sources.

In looking at all the sources, we found that the monitoring covering a number of sites but not all high use areas for the OPs. Even in the largest programs, the ones that had the most intensive sampling, sampling was not frequent enough to account for daily fluctuations. And those programs, all of the programs, also have been done because of constraints of how much they cost for a limited number of years.

Now, I mention that the chlorpyrifos, diazinon, and malathion were the most often included OPs in monitoring programs. But not all OPs were included in monitoring at all. In NAQUA Program included nine currently registered OPs. State programs included some more that weren't in the NAQUA Program, but some of the lower use OPs were not in anything.

Few or no OP degradates of toxic concern were included in most of the studies. Some of the very most recent studies are starting to include those such as the pilot reservoir monitoring study that EPA is doing with the USGS. And the monitoring that was available, even

the most recent data, does not reflect the most recent regulatory actions that were taken. Like I mentioned, voluntary cancellations, although they have been made official, still have the time before they phase in.

So in the end, after looking at all the available monitoring that we had, we concluded that we would not be able to base our exposure assessment solely on available monitoring.

So if we were going to have to make up for the holes in the monitoring assessments, the monitoring programs rather, with computer modeling, this is where the guidance from the SAP we had gotten in the past was particularly helpful. And I'm just really going to run really quickly through some of the highlights of what we learned along the way, what the guidance we received along the way.

In 1997, first taking our model, the PRZM-EXAMS model to the SAP, we were told that it was a good tool, the best tool available, to do our screening assessments. But that in the future, we should devote resources to refining our assessment and concentrate on surface water impacts, and as we go along, to use both modeling and monitoring data in our assessment.

In 1998, we took a first refinement of this model to the SAP, bringing our index reservoir scenario for consideration. This

adaptation of PRZM-EXAMS includes a scenario based on an actual watershed, an actual reservoir, in the Midwest. Then having done that, we moved from working with the watershed to trying to consider what portion of a watershed would actually be cropped to get a maximum idea of what portion of the watershed could actually get treatment by pesticides.

The SAP actually approved of this, especially for major crops. But due to concerns about scale differences, the size of the hydrologic units, the eight-digit HUCs to drive these percent crop area factors, it was not recommended that we use the PCAs for smaller crops or that we considered percent crop treated with the pesticides without getting further monitoring.

Now, this is important. As Nelson will describe before, although the SAP did talk to us about this when considering aggregate assessments, this was something that we felt we had to adopt to some extent in order to do a cumulative risk assessment.

And then one last thing that was on the last slide, the SAP recommended that we consider regional modeling, something that we have done for this assessment.

In 2000, we went further in presenting proposed regression modeling approaches that the USGS was and is developing which show

promise. But, again, it's just another step in the continuing refinement of our assessment. These are still in process. And the SAP recommended that we shift our focus to monitoring programs to support model development and evaluation.

This is led up in December to the case study for the cumulative risk assessment. That used WARP, the regression model; but we were told at the WARP, while showing promise, was not ready for this kind of assessment because it couldn't also do the daily time step. So WARP was not used in our assessment at this time.

Finally, one more please. Something not directly in that line but another ongoing and very important issue that we're looking into is the effect of water treatment on pesticides. And the SAP recommended that until we have enough data for any particular assessment to really know what removal of a pesticide might occur and how much of degradates, especially toxic degradates, might be formed, that we should do our assessments based on raw and not treated water but that we had to consider the impact of transformation products.

This is important for the OPs because we have limited evidence that OP residues are in fact likely to not be reduced. But let me see, the concentration reduced not speaking chemical by water treatment, especially not reduced because we're talking mostly about chlorination

and oxidation processes.

There is, also, evidence for transformation of products that are of toxic concern. However, as consistent with the SAP, because there was not enough information for us to make quantitative adjustments to our assessment, either to figure out how much of the parent goes away, how much of toxic products are formed, and are how long they last, we were not able to quantitatively include the transformation products in, the water treatment transformation products, in our assessment.

So with this guidance in our head, we went forward with a watershed modeling approach for the cumulative exposure assessment. We adapted PRZM-EXAMS in an attempt to estimate pesticide levels in a small drinking water reservoir. By doing that, we derived daily distributions over multiple years with weather being the variable for 12 regional assessments. By doing this, we're able to look at multiple chemicals used on crops in multiple fields within the watershed.

For the cumulative assessment, we adopted typical use patterns, typical rates, looking at the area that is actually treated with pesticides. This is something that we have not done in our individual assessments and we have to actually decide whether it's appropriate to do in our individual assessments.

And, finally, for each of the 12 regions, we looked at region-specific inputs. And I'll describe how we choose our scenarios in just a moment.

Basically, when we decided that we were going to take a look at regional exposure assessment for the cumulative assessment rather than the national assessment that we did before, the first time we considered how we were going to do it we sat around the table and decided what would be the factors that would be important in figuring out what these regions would be. And the very obvious ones that came to mind were the OP usage. It's important to have an regional assessment because some of the chemicals in the assessment aren't used nationally. Some are. But some are used in very specialty crops or just certain parts of the country. So we had to see which crops were there that OPs were being used on and how much was being used.

Then we decided we really need to consider what the source of drinking water is if we're going to do a drinking water assessment. And some parts of the country, say, Florida, Southern Georgia, ground water is the predominant source of drinking water; whereas in other parts of the country, surface water was the main source.

Then we had to consider what the vulnerability of the drinking water sources were. Some parts of the country, while having great OP

use, may not be all that vulnerable to runoff or to leaching. And we wanted to take a look, on a regional basis, what the likelihood of actual vulnerability was.

It just so happened that our friends in the Health Effects Decision knew of a regional framework that had already been developed by the USDA Economic Research Service. These are their farm resource regions and this had the advantage we thought right away of pretty much corresponding with what we were thinking about.

But on top of that, these are based on different farm types and on previous work that the USDA did for separating the country in ways that made sense, both for farms and for climate and for usage. And, of course, they had advantage of ready-made names that we could adopt.

Now, as you look at that, you can see that we have, we have more than 12 up there. We did, in the end, combine some of the regions based on the vulnerability. The basin and range was subsumed into the Northern Great Plains as much as anything because of the amount of OP use and where in that region the most vulnerability seemed to be.

Now, once we had the regions, we still had to determine how to do a drinking water assessment for an entire region. It does represent

a refinement over doing it for the entire country, but it still was a problem that had to be addressed. So in building the cumulative assessment on a regional scale, the first thing we did was to identify high OP usage areas within each of the regions.

You can see, if you look at the regional boundaries, that say in the Fruitful Rim Northwest you have multiple regions that have high OP use, say the Wallamet Valley, the Yakima, and then along the snake river in Idaho. So this was a good first cut.

But then if we go to the next slide, we built on top of that. We took a look at how vulnerable areas were in each of the regions. How vulnerable they were to surface water runoff and something that wouldn't have come through on the computer. You see the dots. On top of the vulnerability, we, also, took a look another where surface water intakes were for drinking water sources.

So taking all of that into account, in the end for the modeling approach, we came up with a set of areas within the regions, watersheds that were going to represent each of the 12 regions. These areas, then, have high apparent potential for cumulative exposure based on the OP use, the number and the pounds of OPs being used in those areas; they coincide with those areas high runoff potential; and where surface is an important source of drinking water.

It is important to recognize that, although we choose those areas to represent the highest cumulative exposure, they don't necessarily represent the areas that have the highest exposure for any single pesticide. But we still expect that the combined OP exposure to be among the highest for each region. And on top of the four regions like the Fruitful Rim Northwest, where we chose the Lamit Valley, we did consider as best we can in our characterization, we attempted to describe other important areas in those regions.

So for the Fruitful Rim Northwest, for instance, we went into a discussion of the Snake River Valley, the geology, the hydrology of the area, the type of use, the source of drinking water, which was ground water. So that in an attempt to try and explain, again, why we thought that the regions we choose were the best representation of risk if the drinking water was a risk driver for any particular region, which as it turned out, they were not, we were prepared to go to a finer resolution than the regions and to try and look at what those watersheds we choose actually represented within those regions and try to get a more refined assessment.

So what we ended up doing by choosing these watersheds was to tailor our assessment to selected areas. We used location-specific enviornmental data for the regions that we chose -- the soil, the sites,

the local weather and the crops that were grown there -- and we considered the major crop OP combinations within that area. And by doing that, we looked at crops that actually occurred together. We were able to look at different OPs used on multiple crops. And if OPs were actually used in those particular regions for usage data. And there the end, we did enough scenarios in an attempt to account for about 95 OP use in each of the areas that we choose.

And Nelson will take over from that to give more details on how we did the assessment.

MR. THURMAN: What I'm going to touch on here is not so much how it built upon the SAP guidance in terms of what we were doing for the individual screening assessments and how we tailored these tools for use in the cumulative assessment. Kevin's already talked about a regional framework, one of the big differences.

If you compare our individual assessments, we started at a national level. We tried to pick one site that represented a high-end exposure across the nation. In this case, we're starting in a regional level and we're looking high-end exposure with each region with a concept of, if we're okay on that site within the region, we're okay in the rest of the region; if not, we need to burrow down further.

I'm going to talk about how we did our watershed-based

modeling and talk about the way we use the data which is a little different than what we have in the individual assessments and how we took a look at usage information.

There some people in this SAP that have been on some of the water SAPs we've had and there are some of you folks are, at least to me, new faces. So I wanted to briefly give you at least a concept of what type of model we were using. For those of you who've heard this, it won't be too long.

Essentially, PRZM, which is the Pesticide Root Zone Model, is something that was developed out of EPA's ORD. It takes a look at what happens when a pesticide is applied to a field. And it basically follows the pesticide from the application to the field to the runoff right to the edge of the water body. It's a field-scale simulation using chemical movement, hydrologic factors. Accounts for ways chemicals are transported, and it is very useful in terms of using it uses a lot of chemical specific. We included both OP pesticide and those toxicological concern it was primarily the sulfone (ph) and sulfoxides.

We did not include degradates that were not formed in the environment, for instance, the oxons were not something we saw in the environmental studies; that is something that we do see as a result of the water treatment. But it is not formed in the environmental studies

we saw.

EXAMS, which is the Exposure Analysis Modeling System, is another model developed by ORD. Basically, it takes over when PRZM leaves off and looks at what happens once the pesticide reaches the water body..

We had a few fixed inputs. The primary fixed input was the geometry and hydrology of the reservoir itself. Essentially, as Kevin mentioned, we used the index reservoir. Essentially, what we did for each of the regions we picked up the dimensions, the hydrology, the geometry, the size, and plot them in each of the regions.

Now this is going to be representative more of drinking water reservoirs and drinking watersheds in the wetter parts of the country than in the west where you're going to need a larger watershed to supply that reservoir. It's also not going to be as representative where you have artificial drainage or controlled drainage conditions, which you also tend to see in the west.

It is a reservoir. It is not a flowing water body. Based on what evidence we have, we expect the reservoirs tend to be a little bit more vulnerable. Once again, we're looking at a site that, if we can make the conclusions we did based on this site, we're not worrying about other sites. But we do no know there were some limitations in terms

of that as we move in different regions in the country. And that's one of the reasons why we continue to go back to feedback on what the monitoring showed.

We had a number of variable inputs. As I mentioned early, the chemistry, chemical properties, were specific to those chemicals. The weather, the site, environmental crop, and usage information are specific to each of the assessments areas. So in that way, we are tailoring to things that actually occurred in the area where we did the assessment.

What you see here, in case you can't see -- what you have is concentration on the Y axis, and you have time on the X axis. And, basically, you're looking at a 10-year span here. What we get as an output of a PRZM-EXAMS are daily distributions of concentrations in water over this ten-year -- in this case, a ten-year period.

I want to contrast a little bit because NRDC raised a concern about one thing we do differently, which, as they pointed out, we use a peak estimate individual screens. Actually, what we use when we do a individual screen is a higher percentile what reflects a one-in-ten-year concentration that we would find over the period.

And I forgot to mention, most of these sites we had up to 36 years of weather data. So we would run this simulation over a 36-year

period. In effect what we're doing when we do these simulations, we're holding use constant and varying the weather from year to year. So the variations you see from year to year reflect differences in the weather and runoff that we get as a result of that.

For an individual screening assessment, we might use this one value. And this red line there. And in effect what we're doing for that assessment is we're assuming that this is a concentration that occurs every day. What we're doing in this more-refined assessment that we're doing and looking at multiple chemicals is we're realizing that that concentration doesn't happen every day. You get your daily and seasonal and yearly variations. So we're capturing that full range of concentrations that you get.

We're also preserving the time component. We do know that in any given year the concentration of pesticide you might see in water on June 1 is going to be related to the concentration you had the day before and the concentration you had the day after. So there is a time relationship that we're able preserve by going to this yearly distribution; and we're able to preserve Calendex to pull those exposures in.

This one did not come out very well. I think we were so ambitious to make sure that you could see it that we overloaded the

memory on the computer.

You should see at second distribution superimposed in here. The intent, the point of that, I can tell you is that with a cumulative, we're looking not just at one chemical; we're looking at multiple chemicals that are going to have uses on different crops; their timing of application is going to be different. We have to find a way to take all of this into account.

Kevin mentioned briefly how as we use the use information and zoomed in on an assessment area in each of the regions, we tried to make sure that we captured all those OPs that would actually be used in the same watershed. For instance, to use as an example, the Northwest Fruitful Rim, we found that OP use on potatoes tend to be concentrated primarily in Idaho. And OP use in apples tend to be more in Washington. So we're not combining those two areas since they don't actually physically occur.

The other component the co-occurrence is the time of use. As I go forward in this, I will try to explain how we did try capture those windows of application so that we could separate that timing as much as we could accurately do with the data we had.

One of the big departures between what we have brought before this SAP in the past and what we were bringing forward in terms of

this cumulative assessment is how we use the PRZM part of the model. PRZM is a field-scale model. That basically carries a lot of baggage with it. It assumes that we can take the field scale and scale it up to a small watershed and not loose too much in the estimates.

We know that there are some assumptions that go with that. We're assuming a single soil in the watershed, the crop and the management practices are homogenous in that area.

For the cumulative assessment, we basically went back and used PRZM as a field-scale model. But what we basically did is we simulated multiple fields in the watershed. One of the things to keep in mind is that, while we did this approach and we feel it's something that does reflect what you might find is happening in the watershed, we still don't have any way of giving a spatial distinction within the watershed.

If you remember in the earlier slide of the pictures, the conceptual drawing of that watershed and reservoir, we basically don't have location-specific information there. We're assuming the crop that's used covers a certain percent of that area, but the percent of area is evenly distributed throughout the watershed. So we're not distinguishing between crops that may be grown in the upper end of the watershed versus those crops that may be concentrated in lower

end.

It also assumes that all of the runoff flows into the water body. We know those are the two limitations that we in that. We do feel that by simulating multiple fields, it better reflected what we needed to do with the cumulative.

We, also, had to have a way to take in the fact that we understand that not all of any watershed is going to be treated with OPs. Those areas that are treated, you're going to have different crops treated with OPs at specific times and specific rates and specific frequencies. I'll say right now, the tools to do that are probably a lot easier to do than getting the data that can do that. And one of our challenges was how to pull this data together and use it to the best we could. And in response to, I think, Daniel Botts comment, we're hoping that we used the appropriate data. And we'll try to explain to you what we did use. And we hopefully used it appropriately as we did that assessment.

One of the things I do want to say is the advantage of simulating multiple fields in a watershed, as we did, is each field may very well have a different soil and a different crop. And so we are getting a little bit more a reflection of a little more heterogeneous watershed than we can using it as we did before.

This picture happens to be in the document and it looks better in color than it does in black and white. Essentially, what I can tell you is that that map shows a percent of the crop areas taking a look at, by on a watershed basis, what the percentage of each of those watersheds are in agriculture.

You can't tell whether the gray tones there, but your highest concentration prejudice of agriculture occurs in the watersheds that are in the Midwest. And the lowest is, obviously, in the Basin and Range. This is where your highest concentrations are.

We used something we've called a cumulative adjustment factor approach to account for the relative contribution of each OP in crop use. We did this in terms that we had to take into consideration both the recommendations and the concerns of the SAP on the percent crop area factor that we brought forward to them. And I'm going to explain to you how we did this so you can take a look and see whether it makes sense. We think it makes sense, but it's one thing we want your feedback on as we go along.

One of things I will say is that one of the earlier recommendations of the SAP was that, when we started looking at percent crop areas, we should do this on a watershed basis. And it makes sense on a physical basis because we're looking at, we're

dealing with watersheds.

The thing to keep in mind the data is collected on the basis of geographical and political boundaries. In other words, most of it is collected at a county or state level, not on a watershed level. So you need to take some way to translate that.

We brought forward an approach in 1997 for applying a percent crop area factor starting with county level ag census data. In the '97 presentation, we used the 1992 ag census. We now have the 1997 agriculture census available which is one of the recommendations the Panel was, as soon as it was out, to use the most updated information.

We, basically, overlaid those with watersheds and used GIS to get that spatial distribution within the watersheds. Kevin mentioned what we had available for GIS were 8-digit hydrologic units, which tend to be fairly large. They average 367,000 hectares in size. And you compare that with 172-hectare watershed we were using, you can see that, at least for the smaller drinking watersheds, you get a lot of them and you can get lost in those large HUCs.

One of concerns of the SAP was that while you may have minor uses that don't add up to a big percentages in these large watersheds, those minor uses are often clustered and they may be clustered in a smaller watershed where they have more of an impact then they did on

a larger scale. So that was one of the challenges we had in trying to convert this data.

We, also, were trying to keep in mind the caution against doing too small a PCA for that reason. What we decided to do is come up with a cumulative OP-PCA. So for each of those 12 regions as you saw, we derived the percent crop areas for the total agriculture using the '97 ag census data.

We then took a look using the latest national agricultural statistics service data which is collected on the county level. We took at look at agriculture land that were in crops that had registered OP uses in that area. And we came up with that percentage. So we essentially adjusted your total agricultural PCA by your percentage of the aggregates from the OPs and came up with a cumulative OP-PCA.

This is an illustration that the numbers you see down there are based loosely on an earlier version of one of the regions we were looking at. I round them off to make it easier for me to do the math and to explain what's going on. One of the challenges we had, if you look at these total acres, they are total acres in the assessment area, which is a lot larger than what you're looking. This is one of the reasons why we went to a percentages so we could use that percentage as a way of scaling down based on the area.

In this particular area, we're looking at a cumulative OP-PCA of 50 percent. Basically, 40 percent of that area in that region were in crops that had registered OP uses.

Now, if you keep in mind that not all -- we know that in any given year, not all of those crops are going to be treated with an OP.

It's further complicated by the fact, if you go to the next slide, that these crops may be treated with multiple OPs. Some OPs may be used on more than one crop. We used a second concept which was a percent acre or percent-acre-treated factor. This basically used the acres treated, which we collected state-level data, as a way of determining how many acres of the total -- for instance, how many acres of total corn were treated with a particular OP.

Now, this acre-treated doesn't take into account the fact that you may have more than one application that goes in that area. And if you were to look over at, for instance, the beans, which you see here, is a particular case we had two different OPs that were basically used on the entire crop at different times.

What's not reflected in here is timing and I'll get at that again in just a little bit. But we used this concept to derive a cumulative acre cumulative adjustment factor which combined both the percent-crop area and the acres treated based on the slide that -- based on the one

that had the map that you couldn't see.

I know you can't read all of these. What I want to just point out is that when we did this, by combining both the acre treatment and the percent-crop area, this gave us a way to distinguish between the relative contributions of each OP and crop use within that watershed. And so we use this cumulative adjustment factor as a way of making that adjustment.

So what we did is that we ended up with each of the crop OP uses that we identified in the assessment area, we ended up with daily distributions. And we still needed to combine these individuals distributions for different chemicals together. So what you see here in each of these distributions is that we put them on equal area. We use a crop-area factor, the cumulative adjustment factor, to put these on equal footing in terms of the area contribution they made in the watershed. We used the relative potency factor, we talked about earlier, to put them on a comparative basis so that we could combine this so that we'd end up with any regions a single distribution over up to 35, 36 years in methamidophos equivalence.

And so what you see there, in fact, you will see in these multiple peaks in a given year, which basically reflect different timings of applications of different pesticides.

Now, there are some assumptions and issues that come out of the way we did this approach. One again, we tried to address the SAP concern about the fact that data came in different scales. We're trying to take county and state level data and apply it to a watershed. And the fact that the size of the watersheds we had that we could work with to do this are a lot larger than the more vulnerable drinking watersheds. And we're trying to address the fact that some of those crops cover small areas.

Our feeling was that by using a cumulative OP-PCA, starting with the total agriculture and adjusting for total OP uses, we don't end up with a number of small, separate percent-crop areas that may introduce more error into it than the combined PCA in that regard.

Secondly, we said we still have some issues on applying an acre treatment adjustment. The percent-crop treated is complied to state level. And there's a couple exceptions in that one is California where they, California Department of Pesticide Regulations, basically has a census in that they require all users to report what they use and when.

The other one is whenever we were looking at the Willamet Valley, we also found some use data specific to the Willamet Valley Collective, actually folks at Oregon State, that we were able to use.

When we take this information to state level and we try to apply

it at a watershed within a state, there's a number of assumptions embedded into this. And one of the big ones it that we've assuming that the data that's collected at state level, the percent-acres treated, is uniform across all watersheds in the state. There's also an assumption of uniformity i time. I'll get to that if in a little bit.

What we know is that pesticide pressures are not necessarily uniform. And so what you're going to find is that where pesticide pressures are great in a particular year, you're going to see more acres treated, possibly at higher application rates. Where they are less, you're going to see less acres treated. So there are some concerns in doing that.

One of the other things as we took a look at that is we, also, realized that crops aren't uniformly distributed across the entire state. So in those areas where your crops are clustered in a certain area and where your use is clustered together, there may be less of a variability than in other cases. And that may be one of the differences between some of the minor crops and some of the crops like corn which tends to be more uniformly distributed in the Midwest.

Our assumption in doing this is that this is probably more of an issue when you're looking at a single crop, single OP use in an single pesticide than when you're looking at an area where you're looking at

multiple crops, with multiple pest pressures that are going to vary, not necessarily all at the same time and over multiple OP uses.

We did take a look in one area to see -- and one effect we got some reflection of maybe some of the variability we might see in this. In the Northern Great Plains we focused on the Red River Valley which tends to be where the highest total OP use was in that region.

We identified high OP use areas on either side of the Red River in North Dakota and Minnesota. As we start taking at look at some of the OP use information, you could see a difference, both in terms of application rates and the percent-acres treated between those two states. Our feeling was that difference was more of a reflection of the data collected at the state level in those two states then of actual differences on either side of the river in that Red River Valley.

We did do comparisons using North Dakota information and then using the Minnesota information to see how much of a difference that makes. And what we did find is that at your highest percentiles -- in fact, anything above 90 percent, there was roughly no more than a 10-percent difference.

And we're talking about single parts-per-billion concentrations, so we're looking at no more than a fraction of a part per billion difference with that. A lot of that was the fact that, once again, we're

looking at a combination of uses. So there was not just one single use that was pulling together.

We used survey data to get at the use. We uses USDAs National Agricultural Statistic Service information on pesticide usage to give us the information on use. We did not attempt to forecast. Except for the fact that we did exclude any uses for which regulatory action has been taken to cancel.

We also focused on the most recent year of the use data. One of things, if you look at the data, and particularly if you look at each of the regional assessments, you will realize that some of those dates -- you have different dates; different years. That's because the NASS collects the information at different times.

Field crops are collected every year, but fruits and vegetables are collected in alternate years. We may have had to go back more than one year to get equivalent data. The other thing to keep in mind what we did use was not your maximum application rate, but we used an average. And that was basically the average of the respondents of the survey within that assessment area.

We took a look -- a number of OPs have more than one method. They can be applied to either aerial or by ground. We focused on the dominant method of application in that area. While our primary source

was NASS, we did, where we could find local sources, we did supplement that information in those local sources and we have documented that in the assessments.

We still need a way to account for the time component of the co-occurrence and in the timing of pesticide applications are going to have a big influence, particularly the timing in relation to when a runoff event occurs.

So we took a look at what information we had. This is a distribution for the Central Valley, California, which we use the in the Southwest Fruitful Rim assessment. This happens to be the area that had the most OP use and the most crops with OP uses.

And as you can see here, you got a distribution of applications the different colors are the different pesticides, have a distribution of applications throughout the year.

One thing to keep in mind is the data in California is a little different than what we had elsewhere in the fact that California does require reporting of every user in terms of how much you used, when, what, where. So we could get that at a county level, and we could get that across the year. So that data reflects more of census than a survey.

And that's the one differences that we had there. This, in effect,

made it a little easier for us to do an assessment in California terms of timing.

DR. BULL: Quick question on that. Those are cumulative curves. I mean you've got one shade.

MR. THURMAN: Yeah. Those are cumulative curves. It may have been easier if we'd had another one where -- but this just shows you the more complex end of it.

In other areas, we only had surveys. So we had to find a way -- we didn't have this type of distribution information. We usually had something tied to a window of application. We had to find a way to find that window in a way that would try to as accurately as we could, reflect those actual differences in applications.

What you'll see when you look at the document is there are different ways we accounted for this temporal variability. In California, where we had the census, it showed a distribution across the year. What we ended up doing was we selected five dates along this distribution with each date representing 20 percent of the total applied use. So, essentially, you had quintals for each of your crop OP combinations.

In the other regions where we didn't have that specific timing, what we usually had was information reported by a particular window.

It was either management windows or times of the year. We used USDA chemical usage information, their planning harvest reports, crop profiles; we talked to regional specialists or local specialists in those areas to try to define that window of the application as narrowly as possible.

If we had a pesticide that had a single application of a crop but we had no distribution information, for instance, if we had a pesticide that we knew was applied at planting, but there was no other information on the distribution of those applications, we would take a look, go to the local area, find out when the window of planing was. And then we would apply this pesticide at the beginning of that use window.

If we had a single application but we had some type of distribution window and we were able to define an active window within that, then we would select the midpoint of that active window to apply the pesticide. If we had pesticide that had multiple applications, then we tried to distribute that evenly across the use window.

Once again, this is given the fact that the information we had. We felt this was as tight as we could get the windows to do that. And given the data scales, it was difficult for us to get tighter values.

There is some conservatism when you saying we're applying all that single application on a given date on the same data in a given watershed as opposed to saying, well, we're going to distribute that application out using a uniform distribution within a use window.

However, we don't think that was unreasonable conservatism when you start looking at the size of the watershed we were looking at. When we're looking at adjusting those fields for the percent crop area and the percent acres treated, it made more sense that these fields were the size that all those applications would actually occur on a single day rather than at different days on there. So we felt like there was some conservatism to it, but it wasn't an unreasonable assumption to make.

What we found is that when we did these and in each of the regions we generally found that there were one or two chemicals that were drivers in terms of the water exposures. This is also in the Central Valley of California. One of things that we found here is these cumulative distributions that we pulled together in methamidophos equivalents, once again, were a function both of the concentration of the pesticide in water and the relative potency factor.

Disulfoton, which is the one that you see dominating the curve, and once again this is a cumulative curve, has a higher relative potency

factor than these other OPs that you see here. That helped skew that curve. We did find, as we went back through there, is that we were able in most of these regions to get some separation of peaks and time so that we weren't artificially adding peaks together that wouldn't actually occur together. And the fact that in each of the regions, we were pretty consistent that there were only a handful of OPs that were drivers. And these tended to be the type of OPs that we saw in the monitoring data suggested that we weren't too far off.

Okay. You'll be happy to know this is the last slide before the questions.

We kept trying to go back and compare what we did in the modeling to the monitoring data. When you look at the report, one of things where the comparison occurs is in each of the regional summaries, each of the regional write-ups we wrote up a comparison. What we're planning to do to make life easier, because of some comments we had, is to try to pull that together in one place for all the regions together to make it easier to find it all at one time.

One of the challenges we had when we were comparing what we did in the modeling to the monitoring is that, A, there is no single definitive study. A lot of the monitoring studies we had were on running water from streams and rivers. There were a few, a couple of

studies, that focused on reservoirs. But these did not focus across a broad geographic range or across a broad time.

We took a look at everything we could. We tried to compare as much as we can, particularly looking at the peaks that we estimated for each of the individual pesticides in those regions to the highest detections that were reported. We also tried to take a look what I would call an "equivalent frequency detection." Each of those, in the monitoring studies, each of those OPs has a limit of detection.

When you're in PRZM-EXAMS, it can carry it out well below the limits of detection. But we could, basically, take a look at what percentile fell above or below that limited detection you would see in the field to see whether or not how we were doing in terms of estimating or overestimating.

One of the things, because they're not necessarily easily comparable, it's difficult to draw definitive conclusions and point this tells us one thing or another. Because we looked at 12 different regions, we were -- give us a chance to take a look at what each region tells us.

So if we were looking at something -- it gives us another way of kind of discerning whether or not we were having a function of compensating errors or fortuitous results or whether we may actually

be on to something.

What we found is the other thing that we need to keep in mind is we did not have monitoring data for every OP. So we had to assume that what we had reflected in comparing for the monitoring that was there would also be have been reflected for the others that weren't monitored.

In each of the regions, we did find a few known detections of one or more of the OPs that occurred at levels that were higher than what we would have estimated. We were looking roughly at order of magnitude differences, in part because the results that we had showed the drinking was and order of magnitude or more lower than food exposure.

So we took a look at order of magnitude differences. And to be honest with you, when you're doing some of these comparisons, getting much closer, gets a little queasy, anyway.

We did find that some of these had reported monitoring values that were higher than what we estimated, but there were also some where our estimations were an order of magnitude more greater than what we found in the monitoring.

We did not find a consistent trend in one way or another. We also found that there were a number of OPs that were fairly close to

each other in each of those regions.

In the questions that you're going to respond to after the public comments, we were asking you about whether you say anything where we may have significantly underestimated exposures, in part, because that's the way the results of the study came out. We're just as interested in anything you see that might suggest that we're significant overestimating exposures, too, so that we can take that into account on future assessments.

And I think the next ones comes to the questions.

DR. KENDALL: I don't want to have those read at this time. First of all, any points of clarification from the Panel for the presentation?

DR. MCCONNELL: I'm sorry. I missed the first few minutes. Maybe you covered this, Mr. Thurman. I noticed in your geography plots up there that one of high use areas is in Florida. And I got to thinking about in a situation where you have soils, poor soils, shallow water tables, have you looked at the ground water; or did you cover that and I missed it?

MR. COSTELLO: We considered it. We made the decision looking at it first -- well, one step back. Again, one of the reasons why we separated regions the way that we did, was to separate those

regions that had ground water as the major source of drinking from those that had surface water as the major source.

Next, we came to the conclusion that surface, generally, would be more vulnerable as a drinking water source to contamination from the OPs. For what data was available, there was clearly a lot more contamination of surface water and, just as importantly, much more cumulative co-occurrence of OPs in surface water. Something that we don't have evidence for in ground water.

But compounding that is the fact that beyond the fact that the monitoring is not enough for ground water to allow us to get the daily distributions, we actually don't have a tool like PRZM and EXAMS that would allow to us do the same thing for ground water. So it is one of the uncertainties of our assessment, especially for places like Florida, that we had to do a surface water assessment and assume that the concentrations that we would come up with, the exposure we would come up with, would exceed it.

There are reasons for certain individual chemicals that calls that into question to some extent. In Florida in particular, one of the OPs has, in certain regions, been found at higher concentrations that we had in our surface water assessment. This is one thing that we describe in our risk characterization as one of our uncertainties.

On top of that, in all of the regions, including the ones in which surface water is the dominant source of drinking water, there is still a significant portion of the population that derives drinking from shallow, private drinking water wells.

Again, this is why we are hoping in the way that we did our modeling scenarios that we have come up with what is likely to give the highest cumulative exposure to OPs as opposed to potential individual higher exposures to individual OPs in shallow drinking water.

MR. THURMAN: One other thing I'd add to that is this is where the relative potency factor also comes into play when we're looking at cumulative impact.

In Florida it turns out that where we did focus on surface water -- and there are not many surface-water intakes in Florida; we know that -- there happened to be a couple of OPs -- and I'm going to blank out on which ones -- that are used on sugar cane that have relatively high application rates and had a much higher relative potency factors than the OPs that we were finding in ground water. So when you started looking at it from a cumulative impact and you take into account the relative potency factor, we did feel that the surface-water assessment is going to be protective in that regard.

MR. COSTELLO: And this is one of the reasons why I described -- when we figured what areas had the highest OP usage, if we had not chosen them to be representative of the entire regions, we made some attempt to characterize the likelihood of drinking-water exposure in those regions. So if you take a look at the Mississippi Portal, for instance, which, like Florida, is an area that has much more of a population deriving its water from ground water than surface water, a detailed discussion of the geology of the area of the aquifers in the area will let you see that the greatest portion of people that derive their water, at least from other than private wells, are getting water that is protected by confining layers between the aquifers.

It does not write off the risk especially to people on private wells. But just to say that we made our best attempt to account for the vulnerability of the drinking source other than the surface water that we used in our models.

DR. KENDALL: Dr. Bull.

DR. BULL: A couple points of clarification. The issue you raise at the end, wouldn't you want -- since this was a conservative approach that you were taking, are you a little bit surprised that you had some things that are higher than what you predicted because I would have guessed this scenario would have been more protective.

MR. THURMAN: We are going --

DR. BULL: I would expected most actual monitoring data to come in lower.

MR. THURMAN: We are going back through and taking a look at each one of those and trying to come up with a rationale, see if can identify a reason why there may have been up.

In some cases, we do know that they are from uses that -- they're uses in the area that are being canceled. So we know that there is that type of a contribution. In some cases what we found that they are in areas were not necessarily, the monitoring was not necessarily directly located where the major use, where our cumulative impact was.

In one or two areas we do find that there were some watersheds where the monitoring came from that are high ag use but are not representative drinking water -- they are not drinking water sources. So those are some of the things we are going back and taking a look at to see if we can...

MR. COSTELLO: But if I may. Some of the monitoring that I did find, although not direct drinking water monitoring, something to keep in mind how limited direct drinking water monitoring is for the OPs. But even if they were not drinking water samples, they were in

potential drinking water sources or in small streams that fed them.

DR. BULL: I'm going to try to keep this to points of clarification.

One of things that impressed me is those areas that you got are pretty heterogeneous within those I areas. I live in one of those areas as everybody else in the room is. But I know what they are.

I heard you talk about weather patterns, but I didn't hear you talk about irrigation. And irrigation is a big issue on runoff because you're going to get runoff from irrigated fields. And if you're just using -- are you taking that into account?

MR. THURMAN: We did take irrigation into account. There were a couple of regions where, you know, PRZM does have an irrigation routine. And in some cases, we've had to do some calibration of that irrigation routine. So particularly in the Central Valley, but in a couple other areas --

DR. BULL: In our part of Washington State, you don't get runoff if it's not from irrigation.

MR. THURMAN: Yeah. To be honest with you, one of reasons why we are looking at that is taking a look at where your runoff was going to occur. And we do realize that -- that's one of things we know that, where you have controlled drainage or human influence drainage,

and in this case irrigation, is this is going to be weaker in terms of trying to capture that effect on it.

DR. BULL: And there's probably limited places you can actually measure it.

MR. THURMAN: Now the thing that helped us on that is we did do -- we were able to do some comparisons from USGS NAQUA data and different -- particularly in the Northwest Fruitful Rim, in each of those major use areas, there were some NAQUA studies that were conducted at the same time. And so we were able to do some comparisons with the monitoring data to see where the relative impacts were likely to be. So that helped guide us in selecting the site.

DR. BULL: There's another kind of issue that runs in a funny way, too. You mentioned the potatoes in Idaho. I've heard -- I'm not sure it's true, but I think we do more potatoes in Eastern Washington than they do in Idaho now.

MR. THURMAN: I apologize for that. But that's true.

DR. BULL: But the issue of shifting crops, I mean, there's also a good -- you can also get applewood which is very good for the fireplace in Eastern Washington because a lot of people are taking orchards and they've shifting to different locations along the river.

MR. THURMAN: Certainly that's --

DR. BULL: How do you take that into account? These are big shifts going on.

MR. COSTELLO: Well, you know, the usage data that we had, the attempt was to have it for as recent as possible, and the monitoring data as well, to keep it somewhat recent. You know, along those lines is why we described how things such as -- we know that the uncertainties say that in the usage that is reflecting a certain number of years that the monitoring can't reflect canceled uses or other OPs that might come in to replace cancelled uses.

DR. BULL: That's what bothered me about taking out the canceled ones.

MR. THURMAN: Once again, we weren't forecasting. But I will say that in each of the regions, as we were looking at the sites, we were laying out what are the crops and what are the uses. And the one that strikes my mind, comes to mind right now, in Eastern Uplands we were looking at an area in Kentucky which did have tobacco use. That is a crop in, at least in Kentucky, is going down in acreage and OP use is going down.

And the other alternative was apples which is in another part of the area which was steady or going up. And so that's one of the things

we did take a look at. It was more of in each of the regions as we're trying to decide where do we focus the assessments. We would look at that, but sometimes that's hard.

DR. BULL: The final question I had along the same kind of line is you said the state usage rates are state wide but you only spread that over crop areas; right? You didn't spread that over --

MR. THURMAN: Only over crop areas.

If you look at the use information that is based on surveys. So they are selecting farmers across the state that reflect -- they're reflective of different farm types and sizes and they're actually asking them what is your application rate, and how many times do you apply it on this. So that survey -- so what we're getting and let's say we get an average is actually a reflection of actual survey response. And it's aggregated at a state level.

DR. BULL: But the apples in Washington, in Yakima, but most of them are probably up in (inaudible) Valley and up in Columbia and up into Canada which is another. The (inaudible) Valley up in Canada. So those are all very concentrated. And then you get out in other areas and they're grains and potatoes and things up on the flat.

MR. THURMAN: Did it does take into that.

DR. BULL: It does?

MR. THURMAN: Yes.

DR. KENDALL: Any further clarification from the Panel about this issue?

DR. CAPEL: Yes. As part of the introduction you showed up a watershed exposure plot for drinking water. I'm not quite sure exactly what that represents. I have two question. One is: Is it the output of PRZM-EXAMS with no adjustments for treatment?

MR. THURMAN: Okay. It's actually more than -- the output of PRZM-EXAMS, we did not adjust the treatment. So basically we're -- we did find anyway to quantitatively do that.

But it also takes into account where Dr. Smith Mr. Dave Miller were talking about the CSFII dietary data. Part of that data includes drinking water consumption. So you get your levels in the water, which are your residue part of that, but you also have a consumption part of that to take into account in that MOE plot that you saw,

DR. CAPEL: So I guess the other half of the question is: Is it based only on the parent compounds, or are the transformation products also included in that?

MR. THURMAN: It is based on parent compounds and transformation products as it occurs in the environmental transformation products. So basically the parents...

DR. CAPEL: So it's part of the PRZM-EXAMS model that you've got --

MR. THURMAN: Yeah, yeah. And there were a couple of other transformation products that were included in there. But those are the major ones that were included in that.

DR. BULL: This is --

DR. KENDALL: Dr. Zeise.

DR. ZEISE: I was wondering if you could speak to the drinking water consumption assumptions that were made. And then how you dealt with it. If we turn back to the food case, it looks as if a good deal of the high-end exposure coming from perhaps high consumption and high residue levels. And I'm wondering if in this example where the equivalent is sort of trying to address that high-end exposure group.

For example, did you address one subgroup that gets basically all it's fluid from water, bottle-fed infant? How did you deal with these more extreme cases?

DR. PERFETTI: As part of the food consumption data, the CSFII survey, the latest one, the 94-96 and even the '98 children level, directly asked the question how much water did the individual drink under those two nonconsecutive days. So those consumption values

are for water the same type, reflecting the same survey that the foods consumption was collected.

DR. ZEISE: Did it capture -- did that sort of capture bottle-fed infant? And did you look at that in particular as a special case where you might have a high exposure? Did you make sure that --

DR. PERFETTI: Water consumption of the bottle-fed infant or the formula consumption.

DR. ZEISE: Well, you would --

DR. PERFETTI: Well, okay. There's two components to water. There's water you get in your food, and there's the water you actually just drink to drink water. Both of those are in the CSFII but in different forms.

DR. ZEISE: Okay. Well, I'm just talking about this one particular subpopulation where you might have very high exposure. Do you think they were adequately captured in this analysis?

DR. BULL: The extreme would be formula made from water.

MS. MULKEY: I thought I understood Dr. Smith as saying -- he's here. Do you know the answer to this question, Bill, the formula that you make up, the power the water in the powder formula.

DR. SMITH: Yes. As I understand it, the current survey, it breaks out the different forms of water, as Randy was saying; and they

are separately listed as water and then there's water that's used in preparing, for example, formula and all the other food components. And it is a fairly high consumption item as you would expect.

DR. ZEISE: Okay. Thanks. As we saw earlier this morning, we looked at different plots for different age groups. And in this case, if you think analogously, this might be an age group where you might see -- I mean, it's very upper tail high levels. And I wonder if you did any of that kind of disaggregation to look to see whether there were some subpopulations that could potentially have higher levels, both on a consumption and then from, perhaps, abnormal use applications.

DR. PERFETTI: Do you mean in terms of the water?

DR. ZEISE: One side the consumption is for the water, and the other side is the different assumptions made with respect to application of pesticide.

My understanding is you've used average application that you obtained from surveying. And I don't know the extent to which that might address things like outbreaks and so forth.

DR. PERFETTI: I'm not sure I understand all of the question. As far as based on the water consumption and the residues observed from the PRZM-EXAMS run, there was none of the subgroups had -- there was hardly any -- well, the MOEs were in order of magnitude

above the food and sometimes three or four orders of magnitude. So you will even -- that subgroup zero to one, which, I assume is what you're referring to, that the water was not playing a major part in that even though, as you pointed out, both from water consumption from the formula plus any water the individual drank would be a high consumption of water.

MR. COSTELLO: And I think understand what you're getting at when you say "the outbreaks." You're talking about pest pressure and using higher than typical rates. And we choose for the cumulative assessment to use typical, that is to say average rates, where we might not before for individual chemicals because we thought it unlikely that the highest rate for each of the pesticides, for all the pesticides on different crops, would be used at the same time.

To attempt to look at -- again, because remember, these are different crops, so pest pressure wouldn't be uniform over all the ones we have in their assemblage. But to attempt to alter some to be higher would introduce another dimension of probabilistic assessment, and it is not something that we attempted.

DR. KENDALL: Any further points? Dr. Portier, you stand, then, between the break and closing this session.

DR. PORTIER: The average rates question, you answered a

question I was going to ask. You didn't consider any variability in what you got out of PRZM-EXAMS. You simply ran it and got sort of an average for each region.

MR. THURMAN: Yeah, actually, that was one thing. We held the application rates constant. So what you see in terms of that variability in time is due to weather differences. There was no attempt to try to -- and, actually, part of the problem is with finding the data to do.

DR. PORTIER: And the other question, since it's not in front of me and one of the questions you're asking us about, is whether we believe that the water component is a trivial part of the organophosphate exposure. I have to ask the obvious question. How bad were your estimates in the worse case? Since I can't see all the data you looked at in deciding the water concentration levels you observed, give me some indication of the magnitude. Is it less than an order of magnitude? Is it two orders of magnitude?

MR. COSTELLO: You mean compared to monitoring.

DR. PORTIER: Yes, compared to monitoring data.

MR. COSTELLO: I think the important -- I could give you a yes-no answer, but that wouldn't be serving you.

In the case of some of the exceedances that were significantly

higher and I think they were at somewhere at least an order of magnitude, you have to consider, again, what the monitoring represents. And this is, again, one reason why we couldn't use the monitoring by itself.

In looking at the available data, it's an assemblage of monitoring studies designed for different purposes. And some of the highest concentrations that we saw, the best example is an area near Salem, called Solter Creek, from the NAQUA program, where there were several of OPs that exceeded significantly when they came up in our cumulative assessment.

But Solter Creek, beyond the fact that it is not a direct drinking water source, also has a small watershed with 99-percent agricultural. Again, a question of scale. The percent-crop-area factors that we come up with are based on OP crops in these large 8-digit HUCs.

So to compare what we come up with there to actual monitoring near the time of application in very high-use area in an area that's got 99-percent agricultural, we have to actually stop and think what does this mean that it exceeded our output.

I mean you have to consider both what does our output really mean, and that's part of one of our questions. And then what does it mean once we figure that out to compare to monitoring with...

MR. THURMAN: With those caveats in mind, I can tell you just from going back and going into a little more detail in each of these and figure out what it is.

In each of the regions, there's no more than a couple of OPs where we found monitoring that was greater. Most of it was around an order of magnitude type if it was greater. It was not much more than that. And once again, at least as I was doing initializing, you look at once we found our overestimates, first of all we found our underestimates and started taking into account the relative potencies of each of those and looking at that. We didn't see anything that suggested a consistent, you know, that we're missing that by an order by what would effect the assessment by an order of magnitude.

I know that's a very general. And I could probably give more details, but I'd have to go back and dig for those.

DR. PORTIER: That's fine. I'm not sure you haven't just answered your own question. But when we get to the discussion, I'll do that.

The other question is the frequency examples. I didn't get a feel for what's the magnitude of the monitored data in terms of, you know, a given region or a comparison to your model. Are we talking about 30 points, 3,000, 20 on an average? Give me some feel for the size of

what you're looking at.

MR. COSTELLO: The very best monitoring that we might have would be a very small area from the NAQUA program, say, bi-weekly over two years. And that's not common. And on top of that, again, then you have to go deeper. Did that monitoring represent target monitoring for OPs? Was it in a high OP use area? Not usually.

DR. PORTIER: Thanks.

DR. KENDALL: Okay. I'm going to go ahead and close this clarification session. We will take a 15-minute break. When we return, we will have two public presentations as registered currently. And then we'll begin the questions at which time the Panel will have full opportunity to address additional issues and concerns.

Thank you.

[Break.]

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